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THE UNIVERSITY OF ALBERTA

SYNTHESIS OF CARBOCYCLES AND HETEROCYCLES BY FREE RADICAL CLOSURE

by

ALI YOUSIF MOHAMMED

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES AND
RESEARCH IN PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE
DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY

EDMONTON, ALBERTA
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"Read in the name of your Lord Who created.
He created man from a clot.
Read and your Lord is Most Honorable,
Who taught (to write) with the pen,
Taught man what he knew not."

(Qurán 96:1-5)

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D. L. J. Clive

Supervisor

External Examiner

DATE 2nd March 1989

To my parents and Hussain

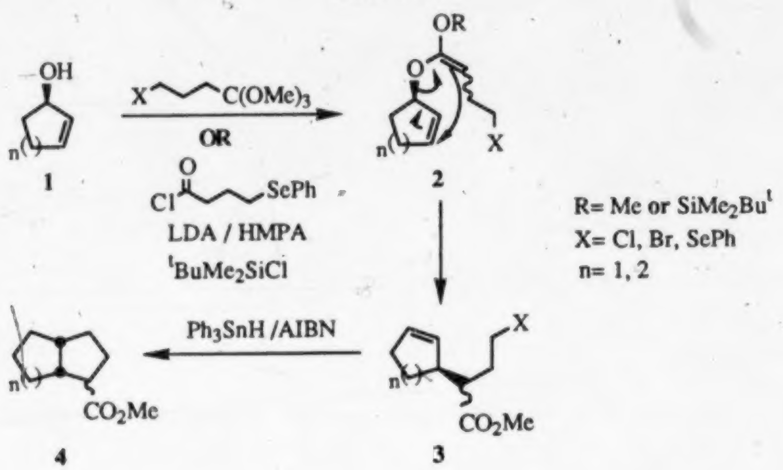
الى أمي وأبي وأخي حسين

ABSTRACT

This thesis describes the development of methodologies in the area of intramolecular free radical cyclization for the stereocontrolled synthesis of 5-membered carbocycles and heterocycles. These reactions are discussed in two chapters.

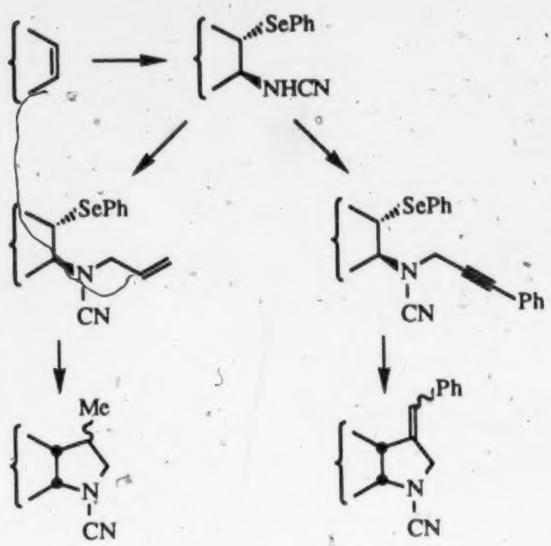
The first chapter describes the preparation of carbocycles from allylic alcohols. The Claisen orthoester rearrangement or the Ireland ester enolate rearrangement followed by radical closure (**3** → **4**) was used to convert allylic alcohols into bicyclic compounds (Scheme 1).

Scheme 1



The second chapter describes an attempt to extend the method to nitrogen heterocycles and this work led to the general procedure for converting olefins into pyrrolidines, as shown in Scheme 2.

Scheme 2



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(I) INTRODUCTION:

i) FREE RADICAL ADDITION AND CYCLIZATION REACTIONS.

Up until about ten years ago free radical chemistry was associated mainly with polymerization processes, but this attitude has now changed and free radical reactions are recognized as very powerful tools in the field of organic synthesis. The area has undergone an extremely rapid expansion. For example, before 1980 only about half a dozen applications had been reported of the use of radical ring closure in the formation of natural products, but since that date dozens of examples have appeared in the literature. Free radical processes are frequently regarded as ideal methods and there are several reasons for this point of view:

1 - Free radical reactions usually occur under mild and neutral conditions.

2 - There is usually no need for protection of hydroxyl or carbonyl groups - situation that is very different from that which prevails in ionic chemistry.

3 - Free radical reactions are not usually influenced to any appreciable extent by the nature of the solvent.

4 - Some free radical reactions are not very sensitive to steric factors, as the transition state is an early one; hence, sterically congested molecules can be prepared.

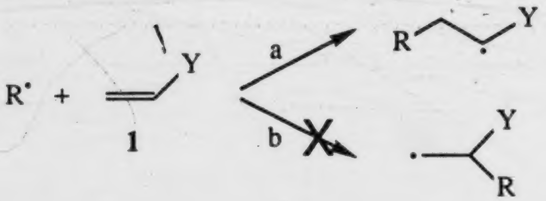
This review will deal with free radical reactions that are stereoselective and will cover their applications in synthesis.

Several reviews on free radicals have appeared in the literature since 1980.[1-11] The scope of the following discussion is divided into four main sections: intermolecular, intramolecular, a combination of inter- and intramolecular reactions and, finally, tandem radical processes. Since the research discussed in this thesis involves intramolecular radical cyclization, this topic will be dealt with more extensively than the other three. For ease of presentation, each grouping is subdivided according to whether a carbocyclic or heterocyclic compound is being formed. To begin with, I present an overview of theoretical aspects related to free radical reactions.

THEORETICAL CONSIDERATIONS:

1- Intermolecular radical additions:

Free radicals add to double bonds in the manner shown in (eq.1).



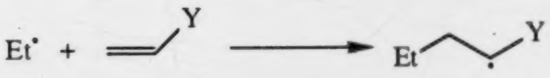
eq. 1

Since the radicals are slightly nucleophilic in character, path b is not favorable. The observed regiochemistry is understandable when Y is an electron-withdrawing group but in other cases the theoretical bases of the preferences is not clear. This kind of addition reaction (eq. 1) has been reviewed extensively[12,13] and only the main features are discussed here.

The rate of the reaction (eq. 1, path a) depends on several factors:

1 - The concentration of the olefin **1**, which usually has to be in a 3 to 20-fold excess.

2 - The nature of the electron-withdrawing group Y. Giese[14] found that the reaction was faster when Y is a powerful electron withdrawing group as shown in (eq. 2).

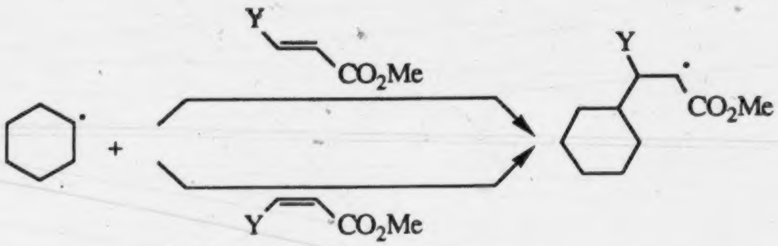


eq. 2

Y	**CN**	**CO_2Me**	**Ph**	**OAc**
rel. rate	5.1	1.9	1	0.05

3 - The nature of the double bond (i.e., whether it is of Z or *E*-stereochemistry, or whether it is internal or terminal).

In this respect, experiments have shown that addition to an *E* double bond is usually faster than to the *Z* isomer. Results of this kind of work are illustrated below in (eq. 3).

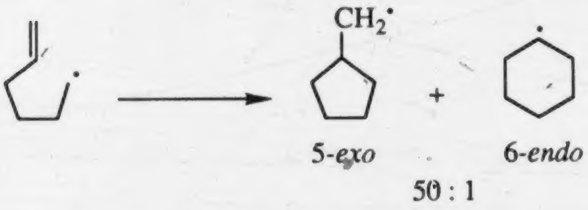


eq. 3

Y =	H	CN	Cl	Ph
k_{trans}/k_{cis}	1	1.4	1.6	5.0

2 - Intramolecular radical reactions:

Intramolecular radical addition (i.e. cyclization) has proved to be very useful synthetically. Much work has been done, particularly by Beckwith, to determine the *exo/endo* ratio,[1-3] (see eq. 4).



eq. 4

The fact that 5-*exo* closure is preferred is due to stereoelectronic effects. The approach of a radical to a double bond has to follow a particular trajectory,[2] (see Figure 1), and this

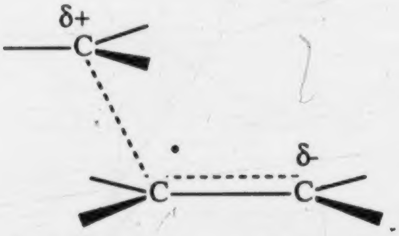
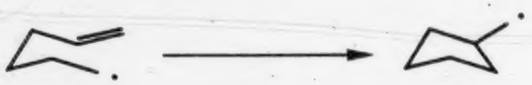


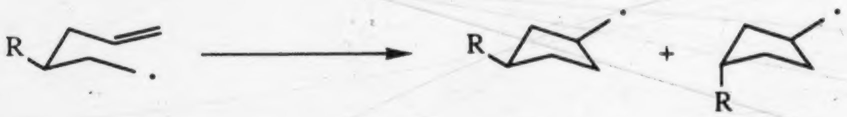
Figure 1. Trajectory of free radical attack on an olefin

trajectory is much more easily accommodated by 5-*exo* closure (eq. 5) than it is by the 6-*endo* pathway. Where the hexenyl radical has



eq. 5

substituents along the chain, the stereochemical outcome of the cyclization is predictable. The assumption is made that the radical adopts a chair-like transition state with the substituents located in an equatorial conformation. Typical results, that conform to this rule, are shown in (eq. 6).

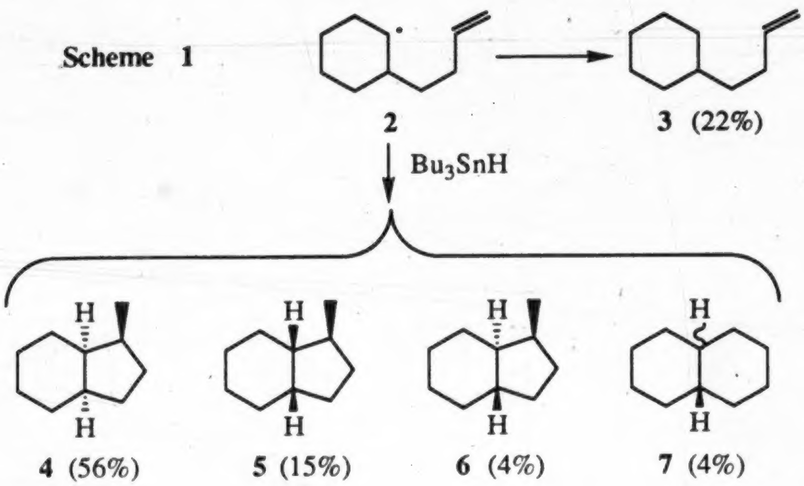


eq. 6

R	k_{cis}/k_{trans}
$-CH_3$	2.35
$-CH=CH_2$	3.30
-Pr	4.50

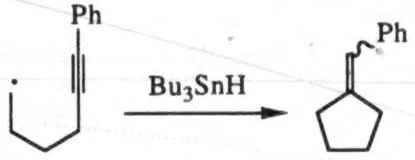
Where the radical is part of a cyclic structure (see Scheme 1) the stereochemical outcome is different. Closure of radical **2** gives compounds **4** and **5** as the major products. On the basis of the above rule, however, one would predict compound **6** to be the major isomer but in fact it was produced only to the extent of 4% (relative). Beckwith has explained[16] that inspection of models indicates that the chair-like conformation of radical **2** in which the butenyl substituent occupies an equatorial conformation allows only poor overlap of the semi-occupied orbital and the π^* orbital of the

Scheme 1



double bond. A much greater interaction is achieved when ring-closure occurs through a conformation of the cyclohexane in which the butenyl substituent is axial. Such a conformation leads to *cis*-fused products **4** and **5**.

Acetylenic systems can also be used in radical cyclization and they have the advantage of producing a double bond in the product so that the result of radical cyclization is a material functionalized in such a way that further manipulations are straightforward (eq. 7).

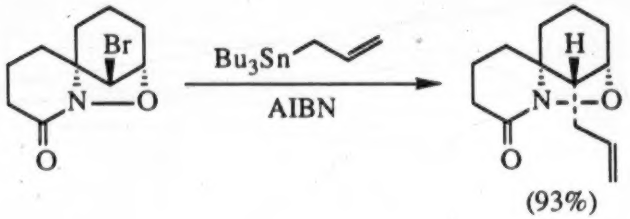


eq. 7

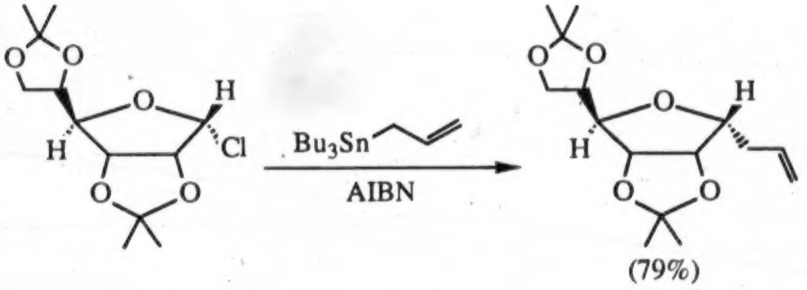
SYNTHETIC APPLICATIONS:

1- Intermolecular Free Radical Addition:

There are very few examples in which intermolecular free radical additions proceed stereoselectively. However, replacement of halogen by an allyl unit using allyl tri-*n*-butylstannane, a reaction studied in detail by Pereyre[17] and Migita,[18] was applied by Keck[19] as shown in (eq. 8). This reaction did occur stereoselectively. Another example, also by Keck, is shown in (eq. 9).[19c]

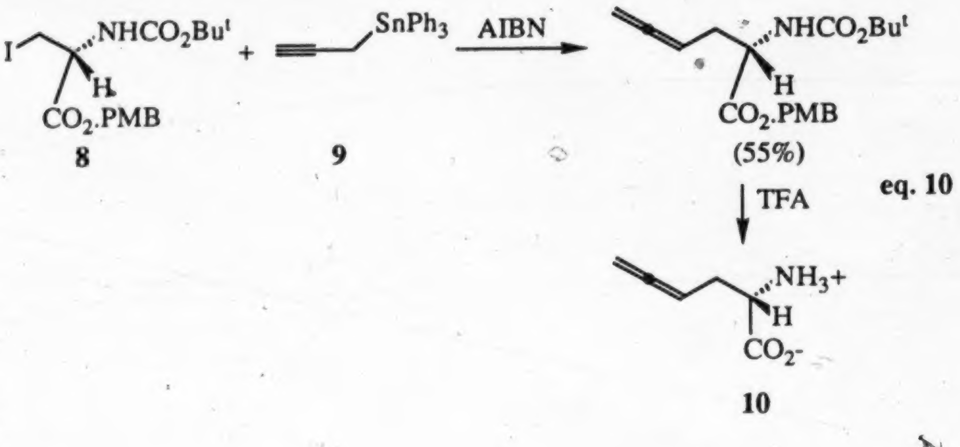


eq. 8



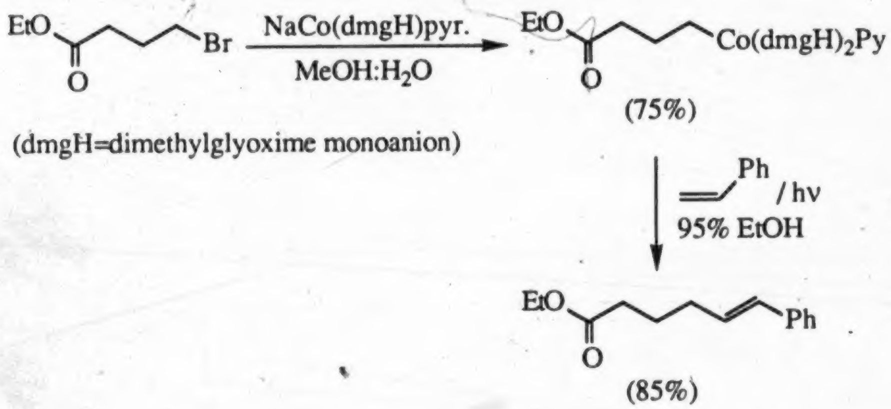
eq. 9

Baldwin[20] reported in 1984 the use of an acetylenic stannane in an intermolecular reaction. He synthesized the naturally occurring allenic amino acid, *S*-2-aminohexa-4,5-dienoic acid **10** (eq. 10) by reaction of the alkyl radical produced from alkyl iodide **8** with stannane **9**. Here, the stereochemistry in the starting material **8** is preserved in the reaction.



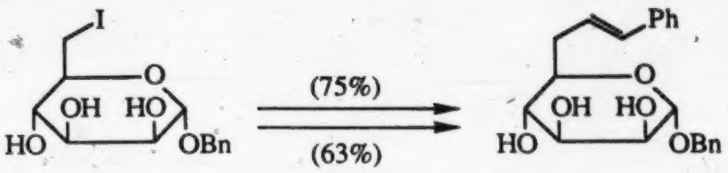
eq. 10

A cobalt-mediated radical addition to an olefin in such a way that the double bond is regenerated stereoselectively was reported in 1988[21] (eq. 11, 12). However, the olefin geometry in both products is the thermodynamically preferred one.



(dmgH=dimethylglyoxime monoanion)

eq. 11



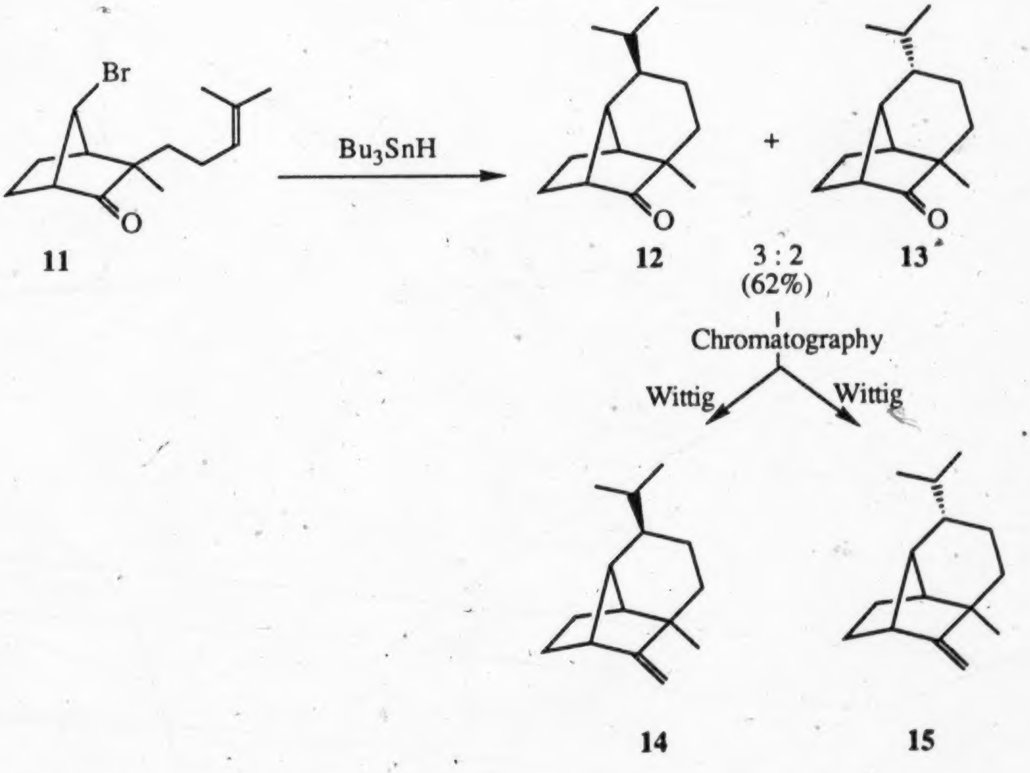
eq. 12

2- Intramolecular Free Radical Cyclization:

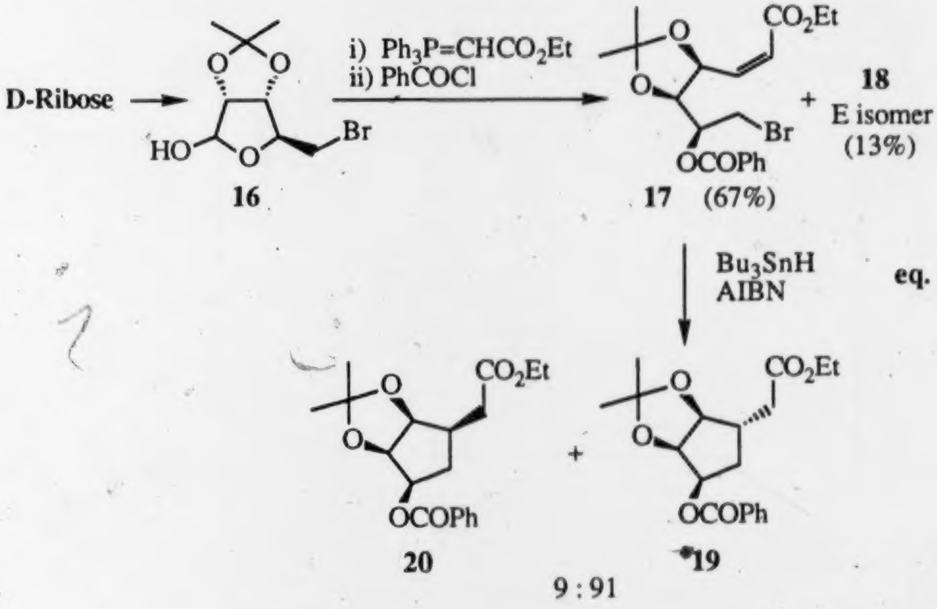
a) Construction of carbocycles:

The first application of radical cyclization in organic synthesis was published in 1976 by Bakuzis[22] (Scheme 2), where the tricyclic sesquiterpenes sativene 14 and copacamphene 15 were produced. This is a good illustration of the utility of this class of reactions.

Scheme 2

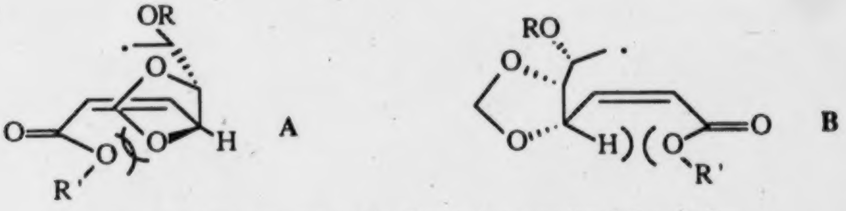


A popular procedure in organic synthesis is the formation of carbocycles from sugars in such a way that some of the stereochemical centers of the original carbohydrate are preserved.[23] Wilcox and Thomasco[24] illustrated the attractive features in this regard of using free radical cyclization. Starting with D-ribose, the lactol **16** (eq. 13) was prepared and, upon Wittig reaction, it produced mainly the *Z*-olefin **17**. Radical cyclization of **17** provided a 91:9 ratio of **19/20** in a combined yield of 89%. The degree of stereoselectivity is among the highest yet observed in radical closures.



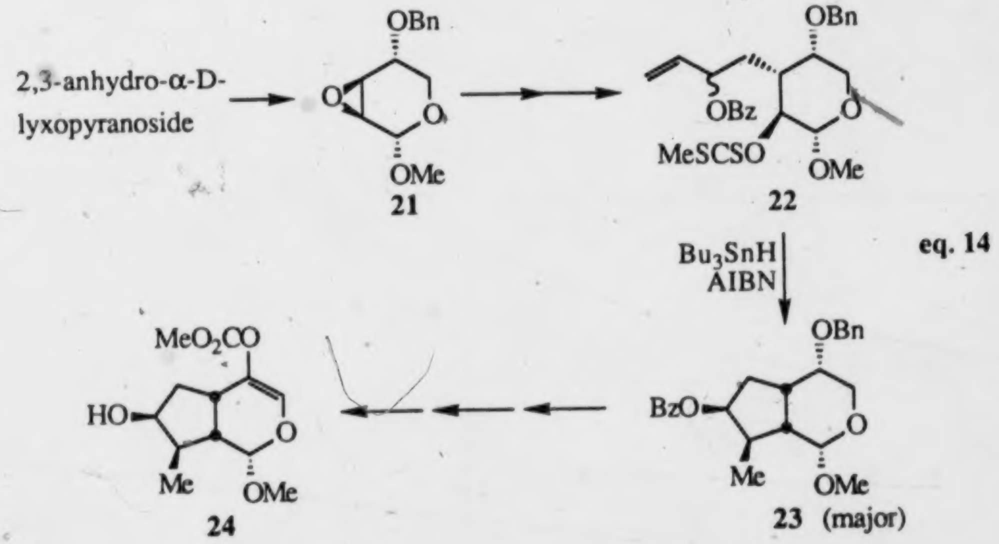
eq. 13

Of the two transition states "A" and "B" for this reaction, that labeled "B" is much more favorable for steric reasons and therefore compound **19** is the major isomer.



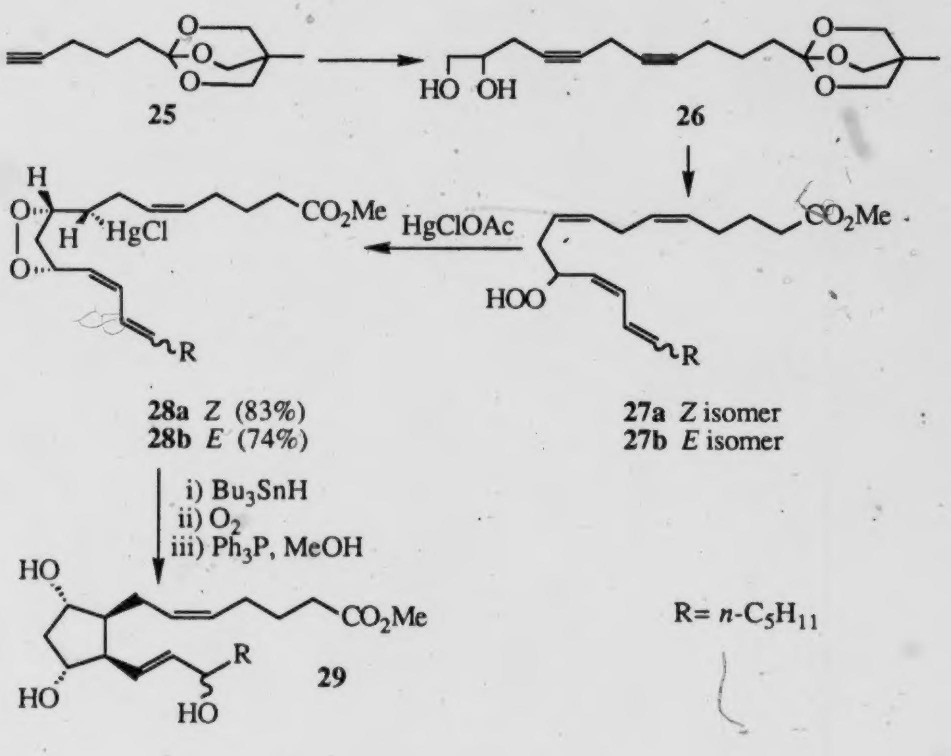
Geminal methyl groups, which have been omitted for clarity, may also influence the outcome of these reactions.

Another example where a sugar is used to make a carbocycle is that of Miwa[25]. He reported the regio- and stereoselective synthesis of 1-α-*O*-methyl-loganin aglycone **24** by radical cyclization as outlined in (eq. 14).

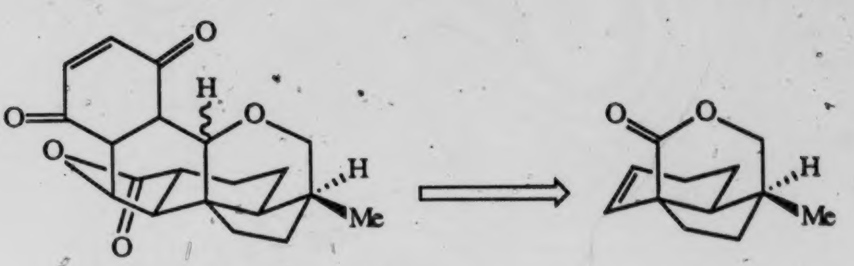


Challenging and complex molecules have also been made by routes in which free radical cyclization is a key step. Corey[26] in 1984 reported the first chemical synthesis of prostaglandin PG_S, using radical cyclization (Scheme 3). The radical cyclization of either **28a** or **28b** gave the same product mixture.

Scheme 3

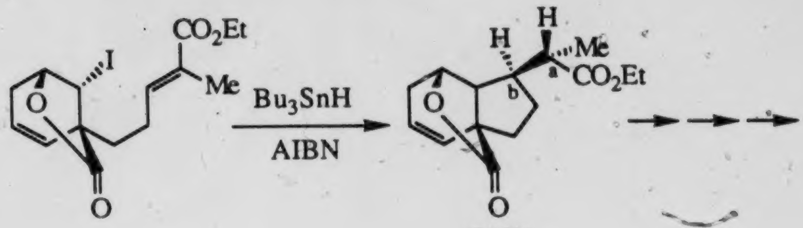


Another application to the synthesis of natural products is the preparation of the tricyclic lactone unit **32** of the antitumor antibiotic pleurotin **30**[27] (eq. 15).



30 β-H **Pleurotin**
31 α-H **Geogenine**

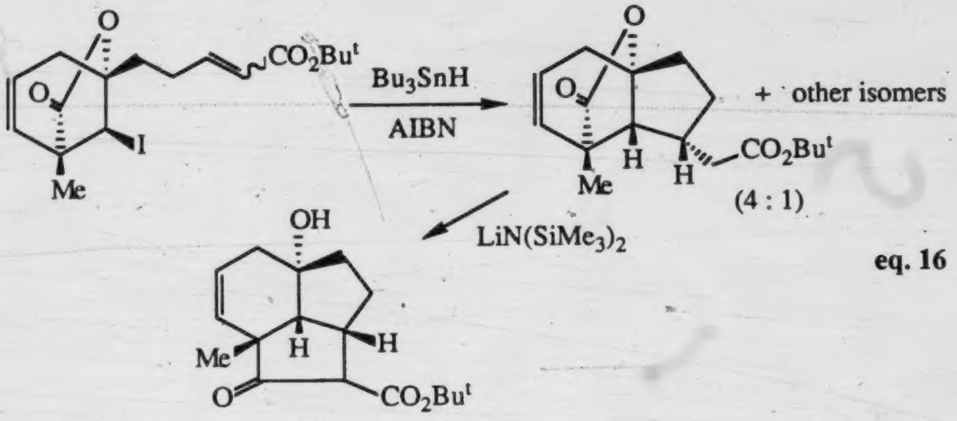
32



(81%)

32 **eq. 15**

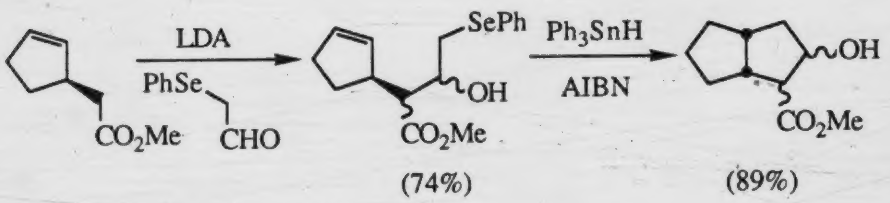
The angularly oxygenated perhydroindane **33** has also been prepared (eq. 16) by radical cyclization.[28,29] The feature of this reaction is formation of a *trans* ring junction in the final 5-*exo* closure contrary to the usual *cis* ring junction. The observed result reflects the preference of a *trans* ring fusion in a 5,6 system over *trans* ring fusion in a 5,5 system. The observed product has the two five-membered rings *cis* fused and only the 5,6 rings are *trans*.



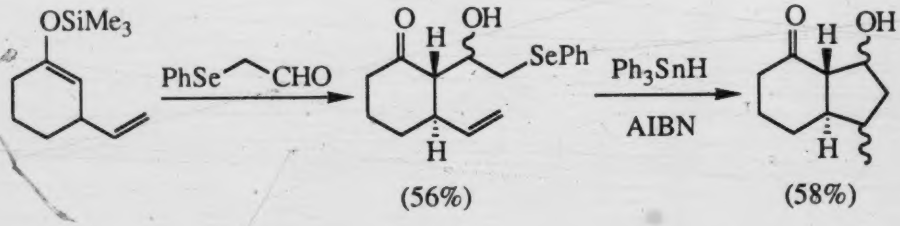
33

eq. 16

Work on radical cyclization in this laboratory started in 1982. Some of the early studies will be discussed later; however, the use of the aldol condensation in conjunction with radical closure was developed here[30] in such a way that either a *cis* or *trans* ring junction can be prepared at will* (eq. 17, 18).



eq. 17

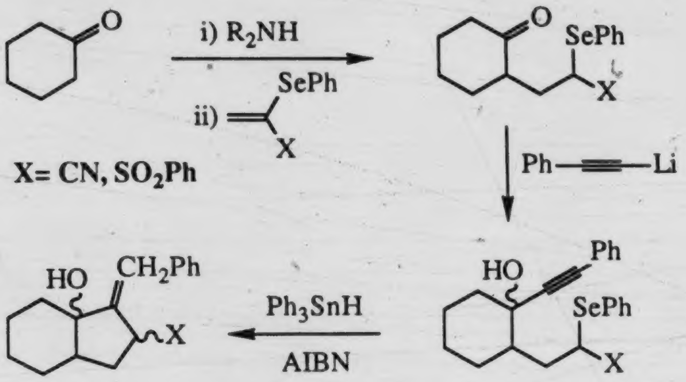


eq. 18

---

* The exception is that in the case of 5-5 ring system, the *trans* ring-fussion is not possible.

The synthetic use of an acetylenic bond to capture a radical was also demonstrated in this laboratory, as shown[31,32] in the example of eq. 19.

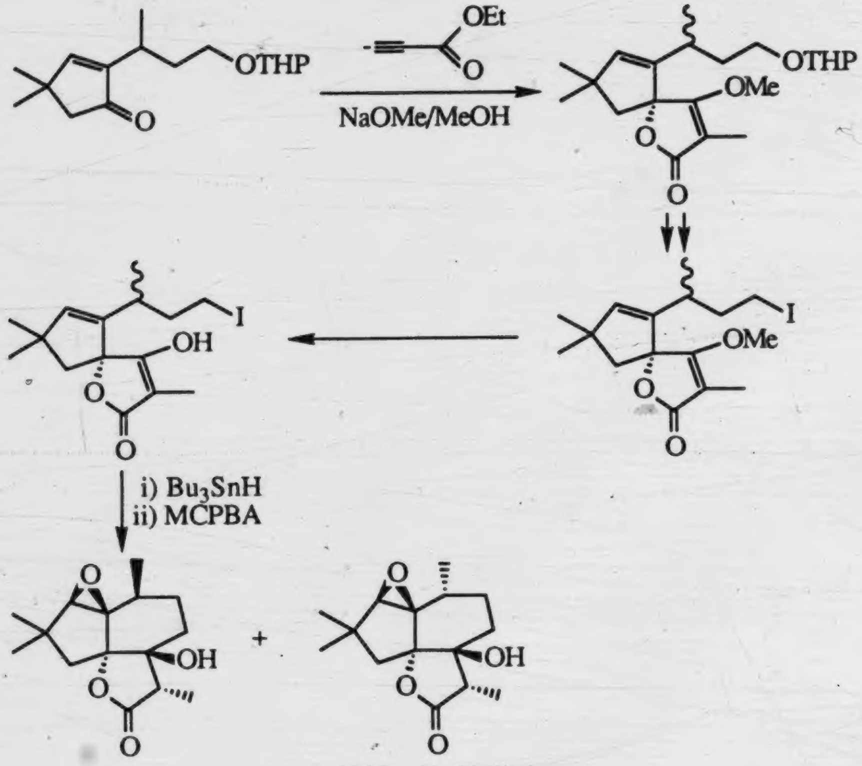


eq.19

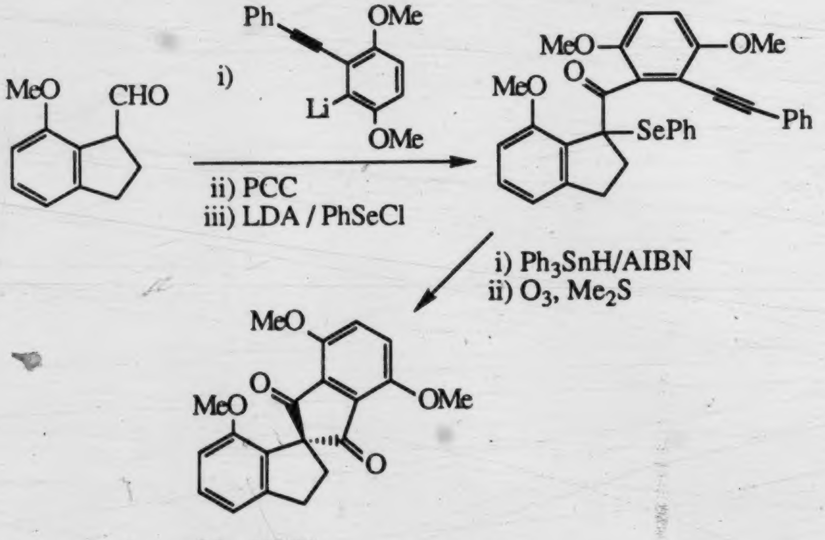
Radical cyclization has also been applied in the construction of angularly fused polycyclic molecules. Pattenden[33] reported the synthesis of the polycyclic alliacol (A) **35** in 1988 as outlined in Scheme 4.

Spiro compounds have also been synthesized by radical cyclization. In this laboratory, a method for the synthesis of this type of compound was established[34] and applied[35,36] to the construction of the central part (**36**) of the biologically active natural product fredericamycin A (eq. 20).

Scheme 4



34 (3 : 1) **35**

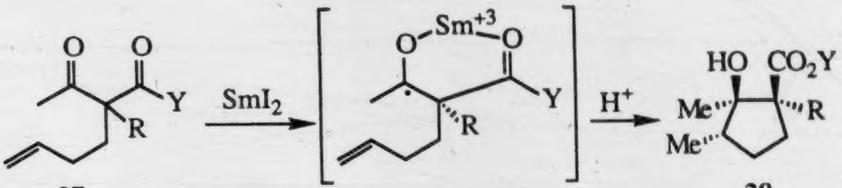


eq. 20

36 (48%)

Beside stannane, lanthanides and transition metals have been used to induce radical cyclization, but these processes are not chain reactions.

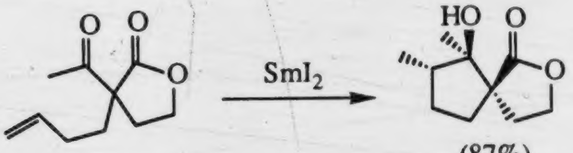
An example of the use of lanthanides is the stereocontrolled intramolecular coupling of unsaturated β-ketoesters and β-ketoamides using samarium diiodide[37] (eq. 21).



37 **38** **eq. 21**

	Y	R	% yield	Diastereoselectivity
a	OEt	Me	(75)	25 : 1
b	NMe_2	H	(78)	> 200 : 1

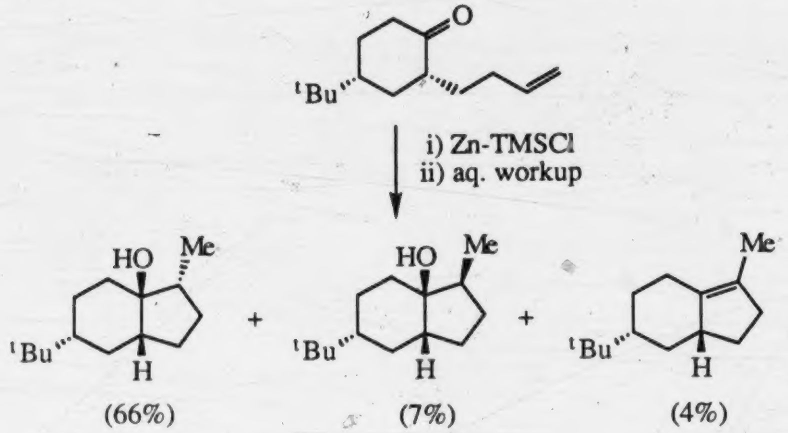
Spiro lactones were also made by this method (eq. 22).



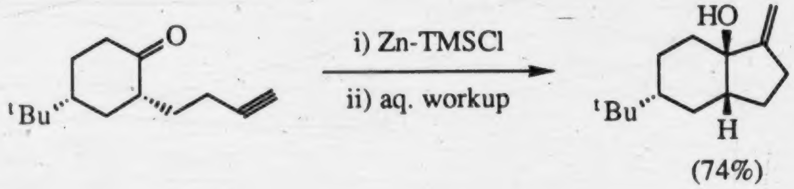
(87%)

eq. 22

The other metal used to induce radical closure is zinc. Corey used zinc-chlorotrimethylsilane with ketones to generate a free radical that can cyclize onto an appropriately located double bond[38] (eq. 23). He also used acetylenic bonds in some of his examples. The use of terminal triple bonds in radical cyclization is sometimes preferred if one need to keep certain functionality in the product (eq. 24).



eq.23

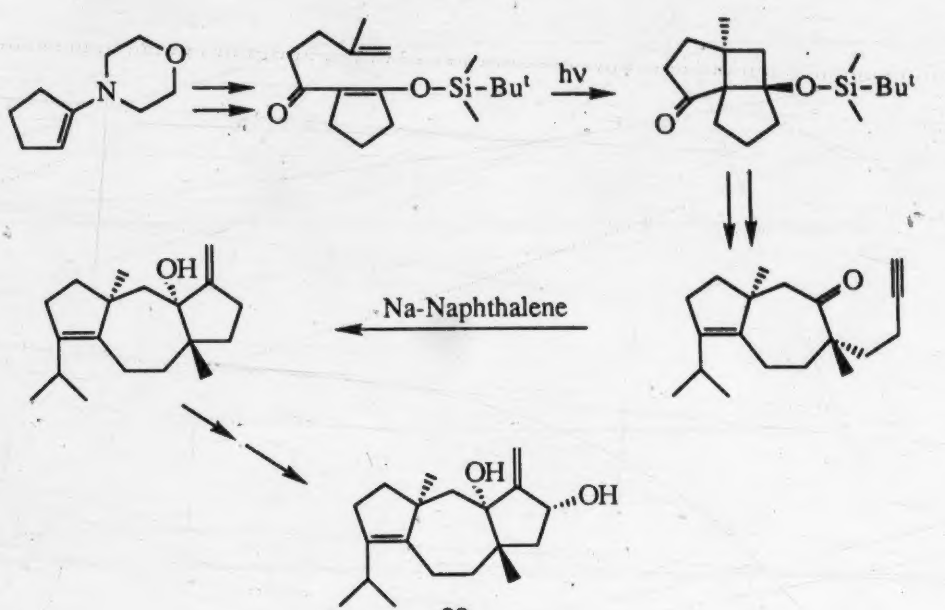


eq. 24

Sodium-naphthalene is another reagent that has been used for non chain cyclization. Pattenden[39,40] used a radical anion, made with this reagent, to induce cyclization in his synthesis of isoamijiol **39**[41] (Scheme 5).

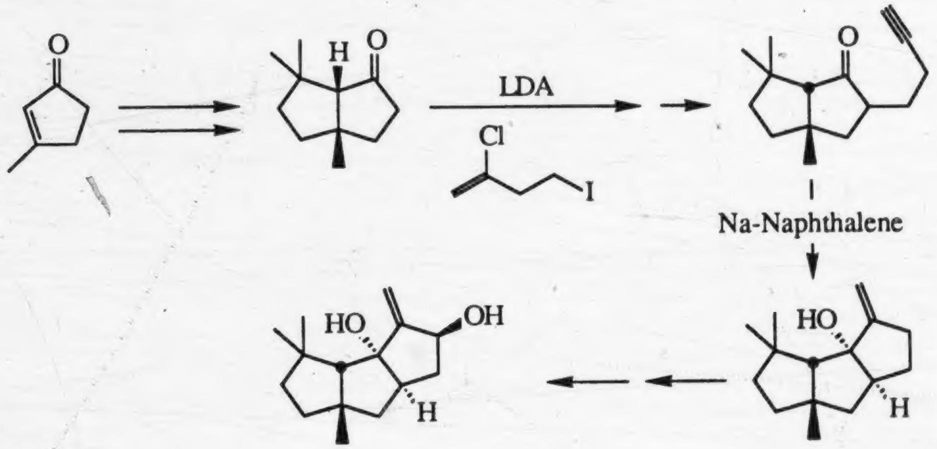
Another example of the use of sodium-naphthalene is the synthesis of (±)-$\Delta^{9(12)}$-capnellene-8β,10α-diol **40**[42] (Scheme 6).

Scheme 5



39

Scheme 6



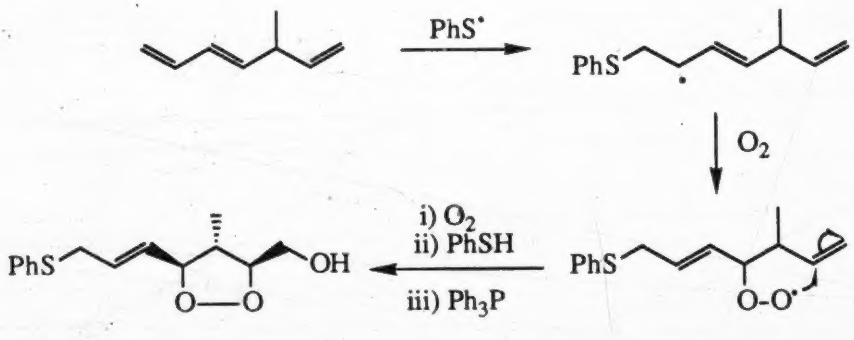
40

b) Construction of heterocycles:

Most natural products that contain rings are heterocyclic. Hence, many procedures have been developed to produce such classes of compounds. Radical cyclization has proved to be very attractive in this area due to the advantages stated earlier.

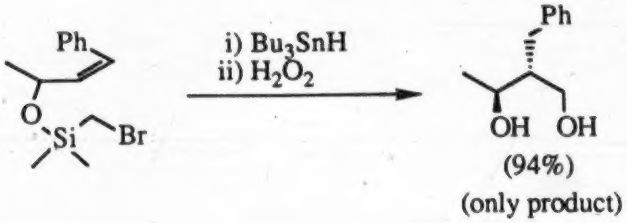
The scope of this part of the literature review will be limited, like the previous part, to a discussion of preparative methods for monocyclic, bicyclic and finally polycyclic compounds.

One of the early reports on using radicals to accomplish cyclization was reported by Beckwith[43] in 1980 in which a stereo- and regiospecific ring closure of an alkenylperoxy radical took place to produce a 1,2-dioxolane (eq. 25).



eq. 25

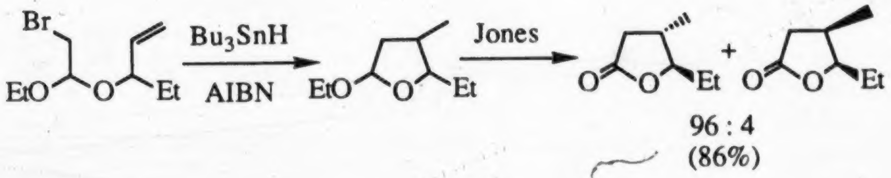
In 1984, Nishiyama reported a stereoselective synthesis of 1,3-diols via silylmethyl radical cyclization[44] (eq. 26). A radical cyclization of (bromoethyl)dimethylsilylallylic esters using Bu_3SnH gave the cyclic silyl ether which, upon oxidation (in a one-pot manner), gave the corresponding 1,3-diols with high stereoselectivity.



eq. 26

γ-And δ-lactones appear in many natural products and many procedures for the synthesis of such compounds have been developed. In this laboratory, the application of radical chemistry to the construction of lactones is being studied and some of the results published will be discussed later when dealing with bicyclic systems.

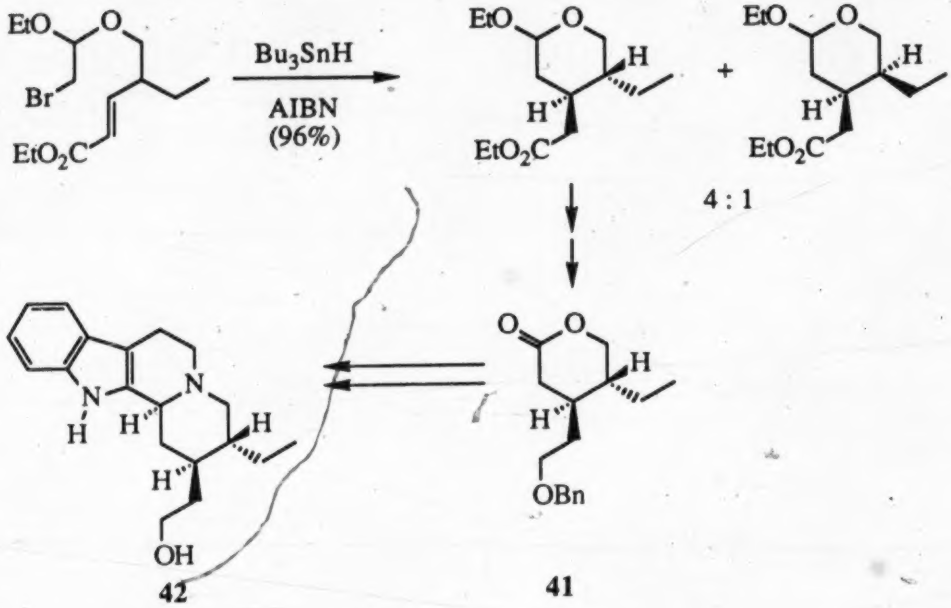
Ueno[45] used 2-bromoalkylallyl ethers as starting materials for radical cyclization to produce lactols, which can be oxidized to lactones (eq. 27).



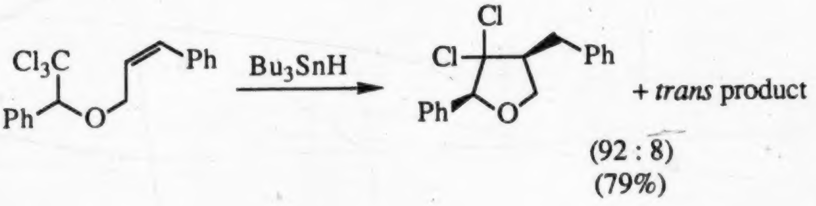
eq. 27

δ-Lactone **41** was made stereoselectively by radical cyclization and converted to (±)-dihydrocorynantheol **42**[46] (Scheme 7).

Scheme 7

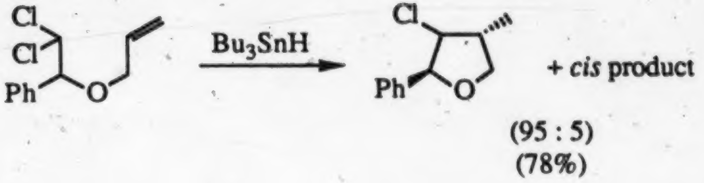


The use of a trichloromethyl group as a source of radicals in a cyclization process showed an unexpected stereoselectivity. Derivatives of 2,2,2-trichloroethyl allyl ether cyclized using tri-*n*-butylstannane in a highly stereoselective[47] manner (eq. 28).



eq. 28

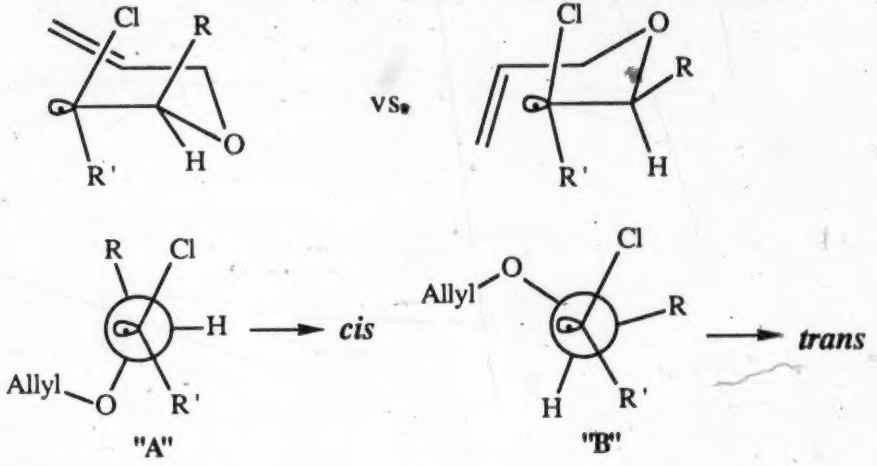
In contrast, 2,2-dichloroethyl allyl ethers gave the opposite stereochemistry (eq. 29).



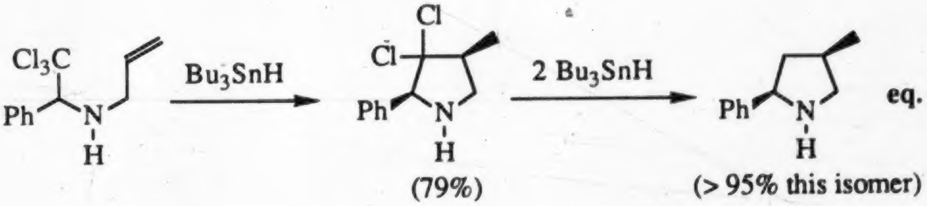
eq.29

The authors explained these results in term of conformatioal analysis (Figure 2). If R' = Cl, A is favored and lead to *cis* products; if R' = H, B is favored and the *trans* isomer is formed.

Figure 2. Conformational analysis of the cyclization of di- and trichloroethyl allyl ethers



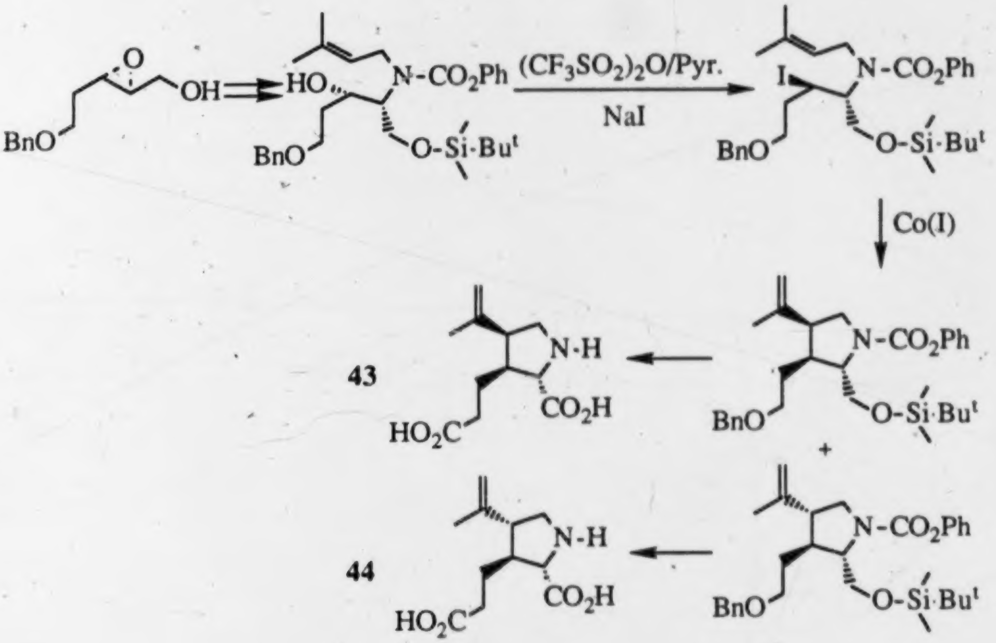
This method was extended from substituted tetrahydrofurans to substituted pyrrolidines[48] (eq. 30).



eq. 30

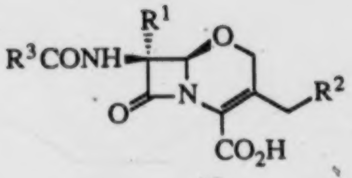
Another example of pyrrolidine synthesis was reported by Baldwin[49] in his preparation of (-)-α-kainic acid **43** and (+)-allokainic acid **44**. In the radical cyclization step, Co(I) was used as a trigger (Scheme 8).

Scheme 8

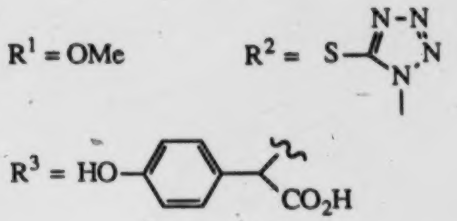


Mainly because of their biological activity and chemical sensitivity, the most interesting and challenging class of bicyclic heterocyclic compounds are those containing β-lactams.

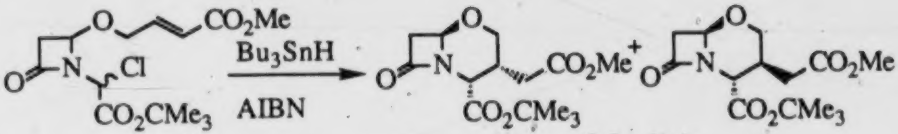
Bachi[50] reported the synthesis of 1-oxacephem **45**, which is the first synthetic β-lactam antibiotic having an unnatural ring system to be used in medicine.



45



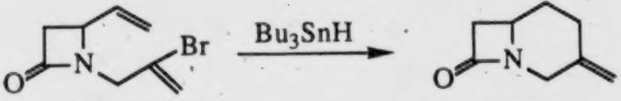
The key step in this synthesis was the use of the radical cyclization shown in eq. 31.



eq. 31

(3.3 : 1)
(68%)

The above radical cyclization proceeded in the expected manner (6-*exo* closure). However, when a competition experiment between 6-*endo* and 5-*exo* closure is conducted, 6-*endo* closure, in this case, will be favorable due to the attachment to the 4-membered β-lactam ring. Hence, compound **46** cyclizes to **47** upon treatment with stannane (eq. 32).[51] On the other hand, Parsons[51]

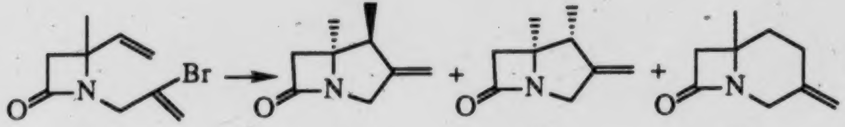


46 **47**

(58%)
(only product)

eq. 32

found that when there is a methyl group at the β-position to the lactam carbonyl, thermal or photochemical generation of the free radical will lead mainly to 5-*exo* closure (eq. 33).



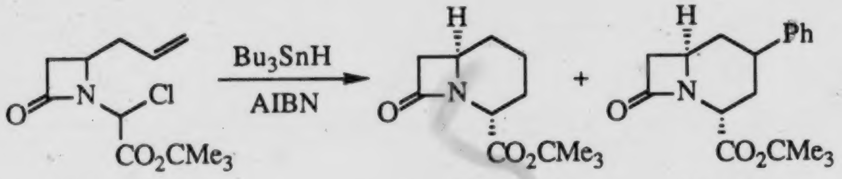
eq. 33

48 **49** **50** **51**

	49	50	51
Δ	59%	3%	30%
hν	58%	10%	10%

Parsons also found[52] that the thermal reaction of **48** is concentration dependent. At a very low concentration of the substrate, 6-*endo* closure is the only pathway, but at ca. 8-10 mM concentration, the product of 5-*exo* closure was the only one formed.

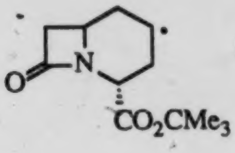
At about the same time, Bachi was experimenting with similar systems. He found that compound **52** produced only products arising from 6-*endo* closure[53] (eq. 34). Compound **54** was obtained



eq. 34

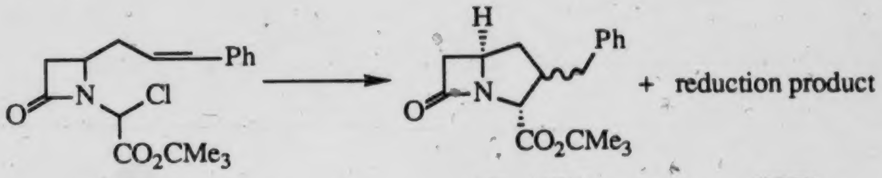
52 **53** (50%) **54** (14%)

from a homolytic substitution of radical **55** on benzene, which was used as solvent.



55

Surprisingly, compound **56** produced products arising from 5-*exo* closure (eq. 35).



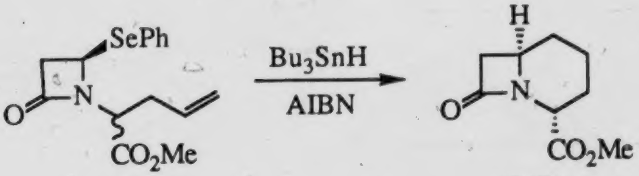
eq. 35

56

57 (62%) (20%)

Similar results arise when using an acetylenic instead of an olefinic pendant in the radical cyclization.[54]

Very recently, Kametani has found that the use of a phenylseleno group as a radical generator at the 4-position (eq. 36), proved to be superior (59%) to use of the corresponding phenylthio derivative (40-45%).[55,56]

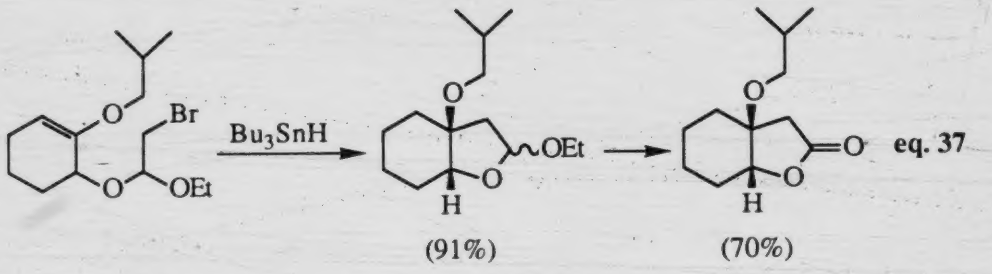


eq. 36

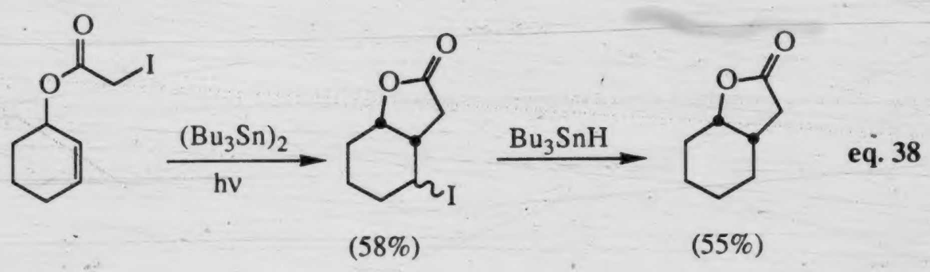
(59%)
(only product)

As stated earlier, γ-lactones have attracted much attention from synthetic chemists and the next few examples will deal with methods that use radical cyclization to generate γ-lactones.

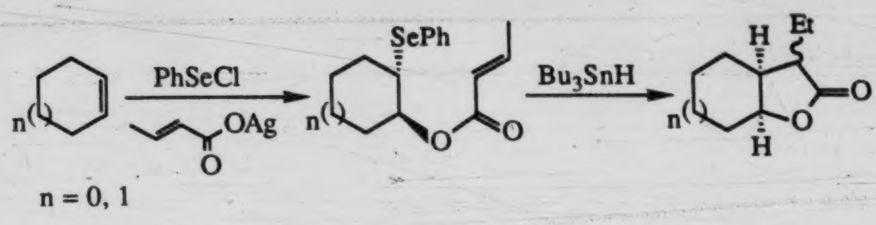
Pattenden devised a method (eq. 37) to make protected lactols that could be oxidized to the lactone afterwards.[57]



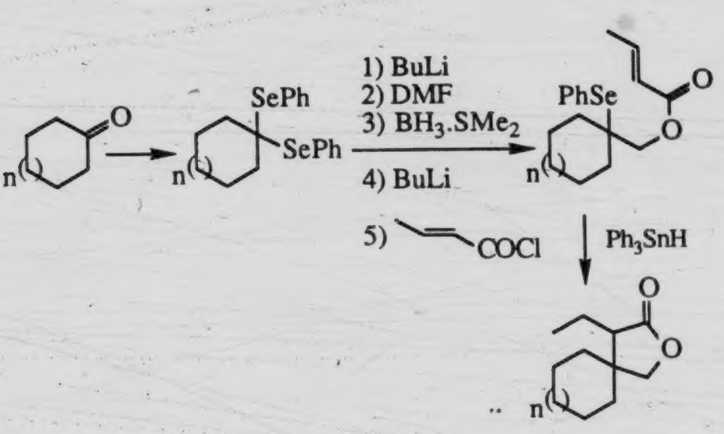
Curran used a more direct approach based on atom transfer[58] (eq. 38).



In this laboratory, two routes were developed to γ-lactones[34,59] (eq. 39, 40).

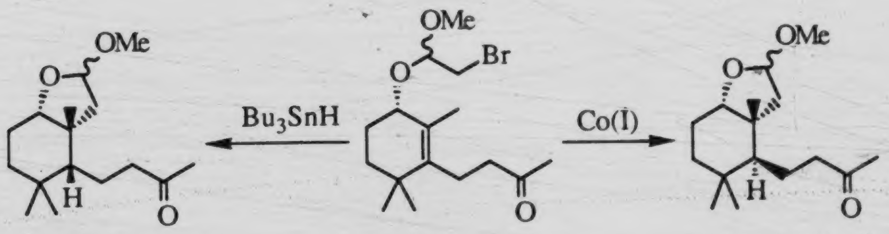


eq. 39



eq. 40

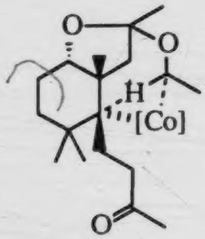
Pattenden noticed that the stereochemistry at the α-position to the ring junction can be controlled at will when the agent producing the radical is changed.[60] He found that using a stannane with compound **58** gave protected lactol **59** (eq. 41), which can be converted to lactone; while a Co(I) reagent gave the opposite isomer **60**.



59 (95%) **58** **60** (70%)

eq. 41

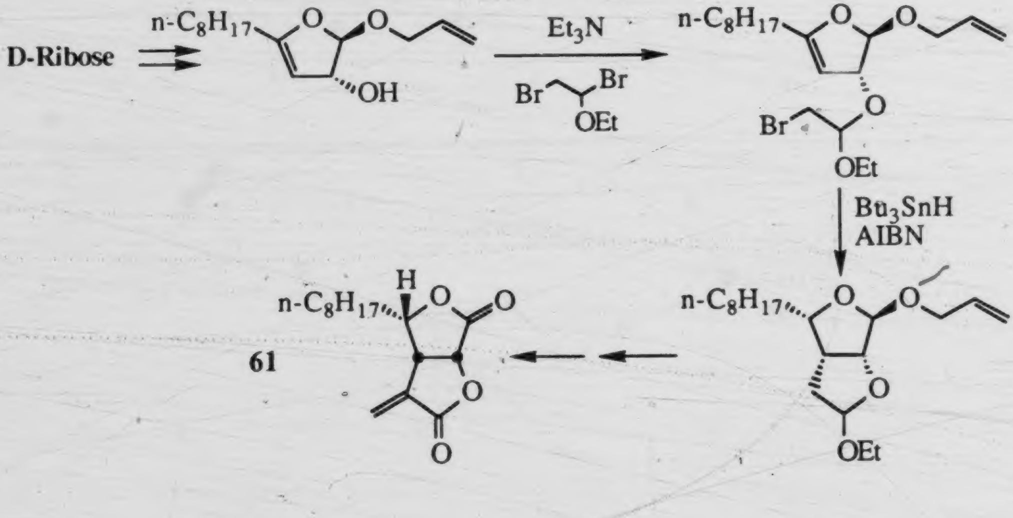
The reasons for these observations are not known yet, but apparently the two reactions proceed by different mechanisms; the cobalt reaction, evidently, involves a type of intermediate that facilitates an intramolecular hydrogen transfer as shown in **60'**.



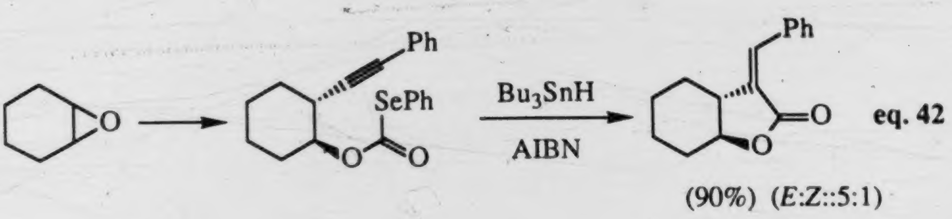
60'

These developments in radical cyclization have lent themselves to the synthesis of some naturally occurring compounds. The antifungal mold metabolite, (-)-isoavenaciolide **61**, was synthesized from D-ribose[61] (scheme 9).

Scheme 9

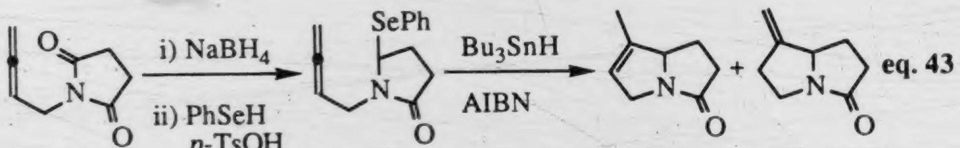


Bachi also made a contribution in the γ-lactone area by synthesizing α-alkylidene-γ-lactones.[62,63] These γ-lactones, which are fused to six- or seven-membered rings, were prepared by a method that gives the *trans* ring junction (eq. 42).



Nitrogen heterocycles are also important in natural products and the preparation of pyrrolizidinones, pyrrolidines and dihydropyrroles will be illustrated below.

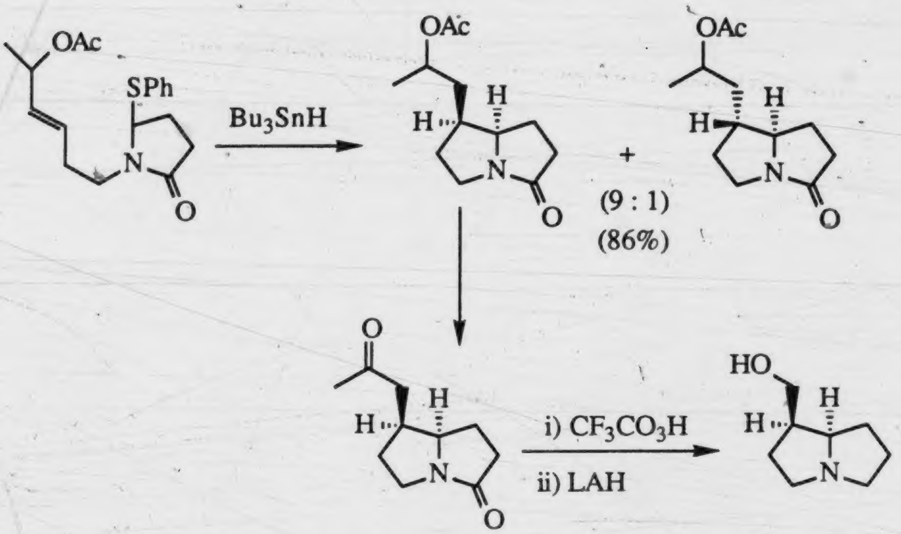
Cyclization of a free radical into an allene (eq. 43) produced the pyrrolizidinones **62** and **63**.[64]



62 (52%) **63** (14%)

Another example of these techniques was reported by Hart[65] in which he made the alkaloid isoretronecanol **64** (Scheme 10).

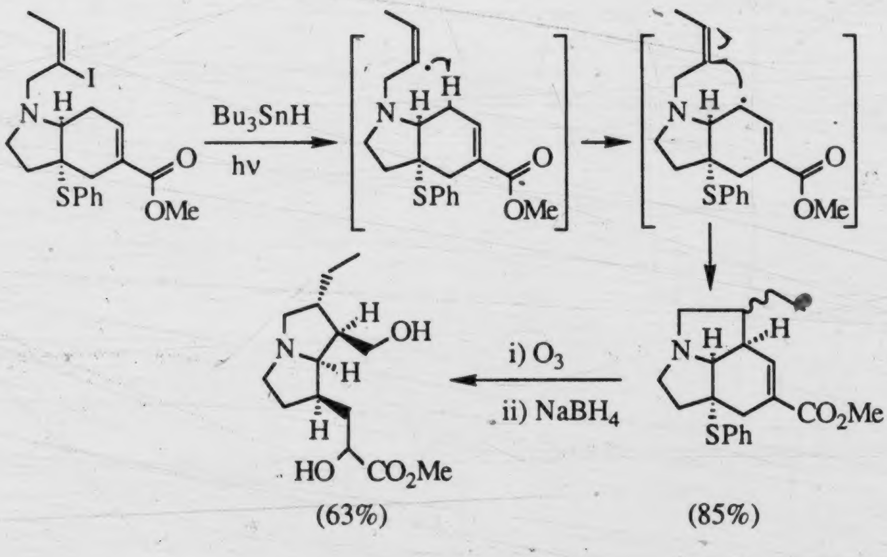
Scheme 10



64

Keck and Enholm also prepared **64** in a similar fashion.[66]

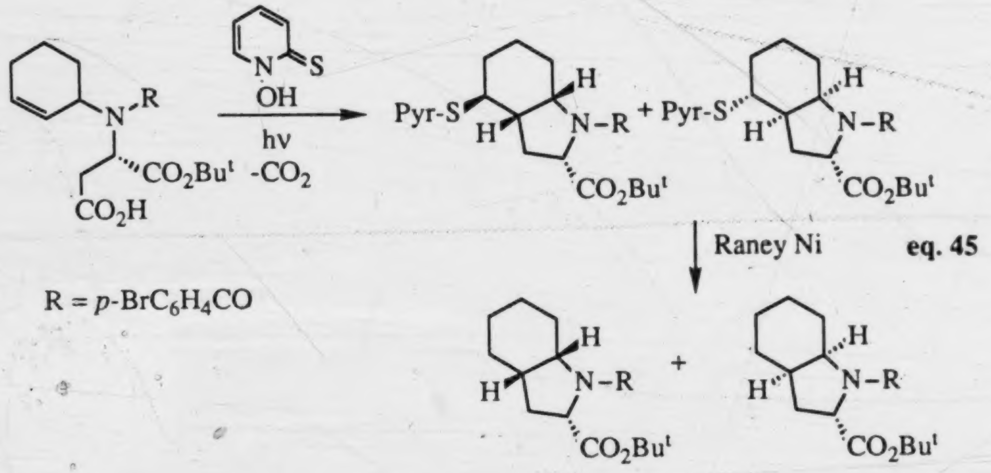
Pyrrolizidine rings have been made by a method in which a vinylic radical abstracts a hydrogen atom intramolecularly via a 6-



eq. 44

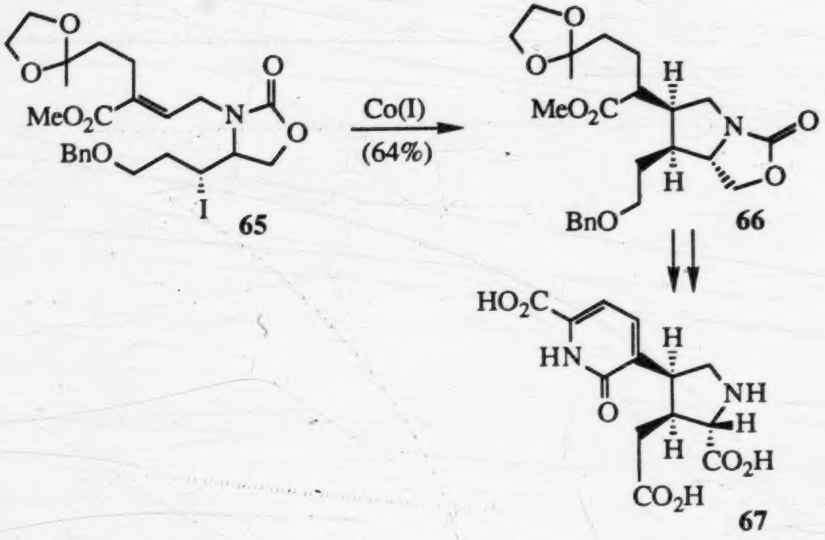
membered transition state to generate a new allylic radical. This, in turn, cyclizes onto the olefinic bond to produce the pyrrolizidine ring[67] (eq. 44).

Barton used a photochemical method to make the pyrrolidine system[68] (eq. 45). In his approach decarboxylation is used to generate the free radical, which then cyclizes to the desired product.



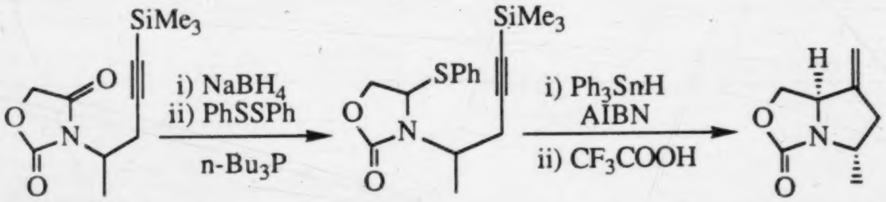
eq. 45

In the synthesis of natural products, Baldwin prepared Acromelic acid A **67**.[69] This acid is isolated from the poisonous mushroom *Clitycybe acromelalga* and possesses extremely potent depolarizing activity on glutamate-mediated neurotransmission. The key step in this synthesis was the successful conversion of **65** to **66** by metal mediated radical cyclization (eq. 46).



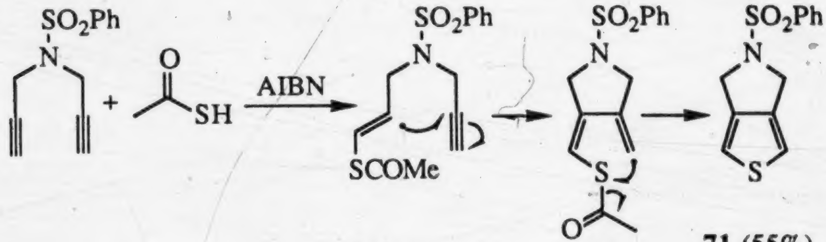
65
66
67
eq. 46

Apart from double bonds, triple bonds have also been used in radical cyclization. Kano reported[70] a simple diastereoselective synthesis of tetrahydropyrrolooxazoles using a triple bond to capture the radical (eq. 47). He described the conversion of oxazolidine-2,5-dione **68** to 4-(phenylthio)oxazolidine-2-one **69**. Upon treatment with stannane reagent and desilylation this yielded the desired product **70**.



68 **69** **70** (72%)
eq. 47

Padwa[71] reported radical addition of thioacetic acid to *N*,*N*-bis(2-propynyl)benzenesulfonamide to give the dihydropyrrole derivative **71** (eq. 48).

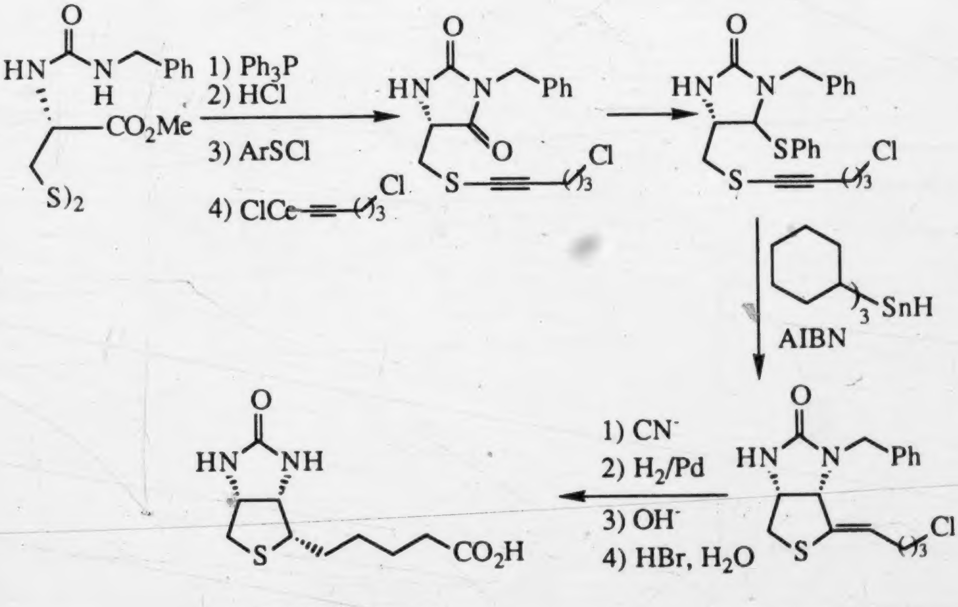


71 (55%)

eq. 48

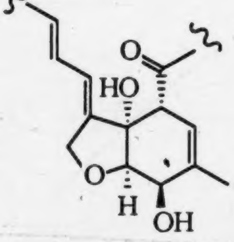
(±)-Biotin was synthesized enantioselectively and stereospecifically from L-cystine dimethyl ester[72] (Scheme 11).

Scheme 11

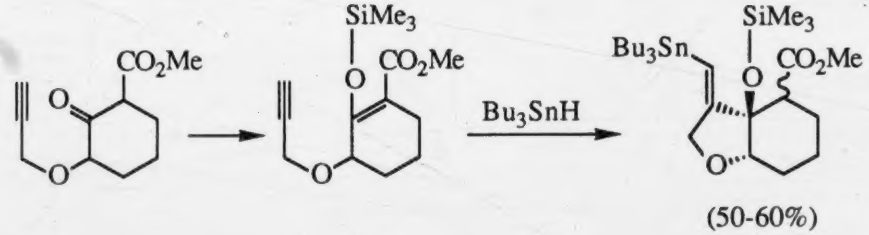


(+)-Biotin

Julia in 1987 reported a model study towards the synthesis of the lower portion of Avermectin B_{1a} using radical cyclization methodology[73] (eq. 49).

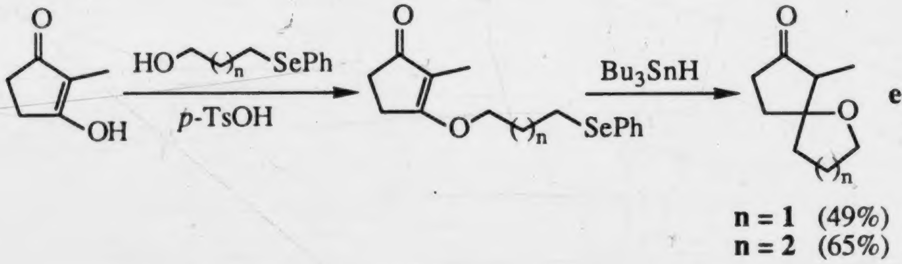


Lower portion of Avermectin B_{1a}



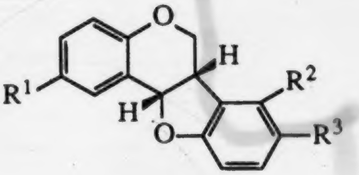
eq. 49

Spiroethers have also been made by radical cyclization[74] (eq. 50).



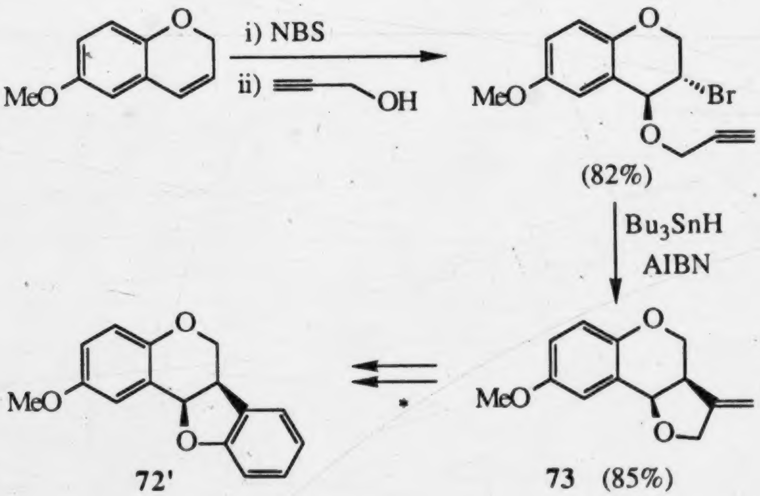
eq. 50

Polycyclic heterocyclic systems are also accessible using radical techniques. Pterocarpans[72] are a wide range of compounds produced by *Leguminosae* plants when challenged by fungal



72

infection. Synthesis of two of these natural products will be discussed. In the first one, compound **72'** (R_1=OMe, R_2=R_3=H) was produced* from **73**, which was made by radical cyclization[75] (eq. 51).



eq. 51

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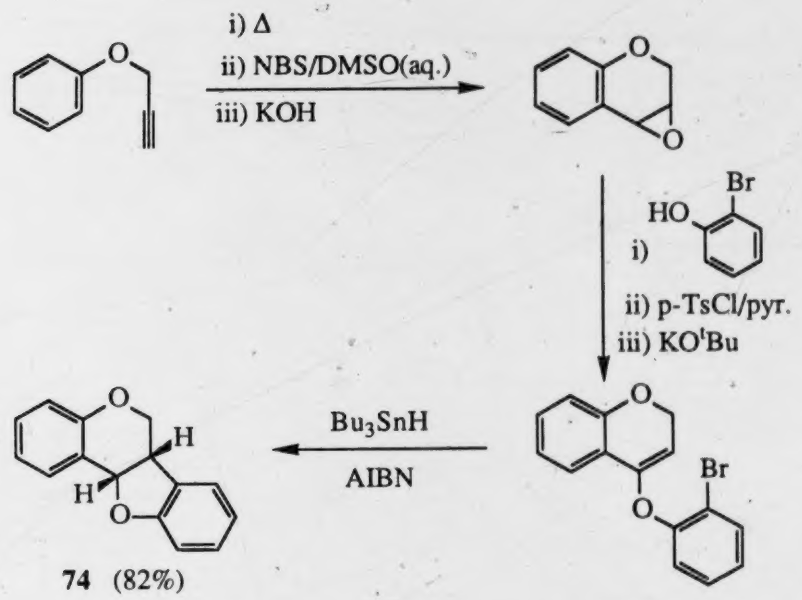
* The literature describes **73** as a potential precursor for **72'** but does not indicate how the transformation is to be accomplished.

The second compound, 6a,11a-dihydro-6*H*-benzofuro[3,2,-c]benzopyran **74** was synthesized by radical cyclization in an apparent 5-*endo* closure, which is a forbidden mode of radical closure. However, the authors did not comment on this particular result[76] (eq. 52).

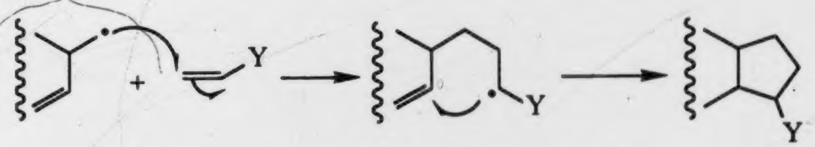


74 (82%)

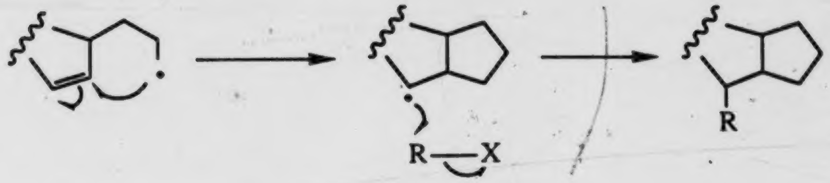
eq. 52

3- Combination reactions:

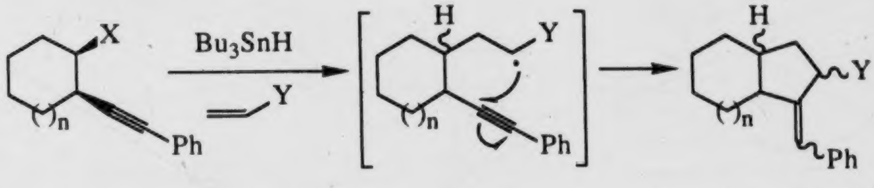
A combination of inter- and intramolecular radical reactions (eq. 53, 54) has been also studied, but to a limited extent.



eq. 53

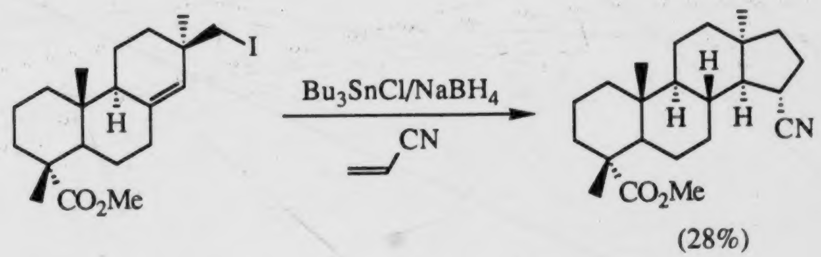

eq. 54

The first example in alicyclic chemistry was reported by this laboratory[77] (eq. 57).



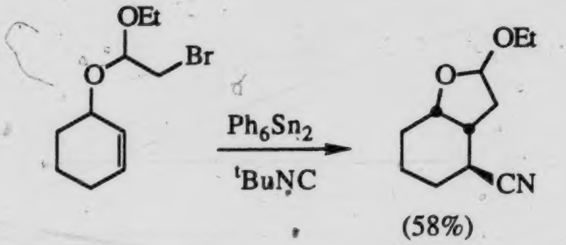
eq. 55

Ring D of steroids (but with C/D *cis* fusion) was synthesized by intermolecular addition followed by intramolecular cyclization[78] (eq. 55).



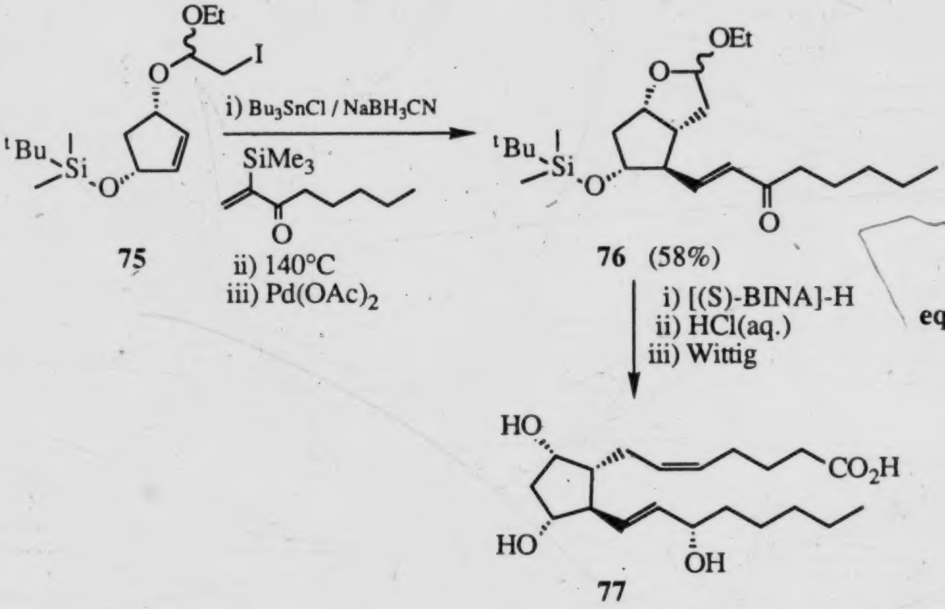
eq. 56

Stork, however, used the reverse methodology whereby he had the intramolecular mode of cyclization first followed by intermolecular addition. This method is illustrated in (eq. 56).[79, 80]



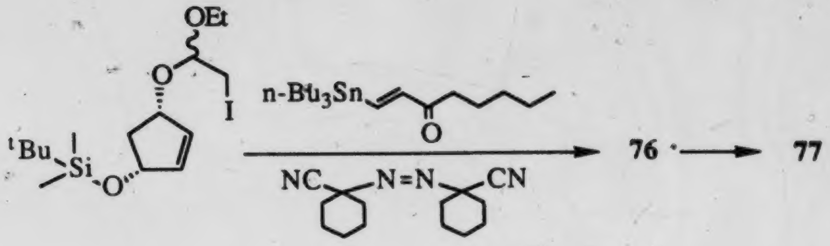
eq. 57

Stork applied his method to the preparation of the natural (+)-prostaglandin $F_{2\alpha}$ **77**.[81] This intramolecular radical cyclization-trapping methodology proved to be very efficient and stereocontrolled[82] (eq. 58).



eq. 58

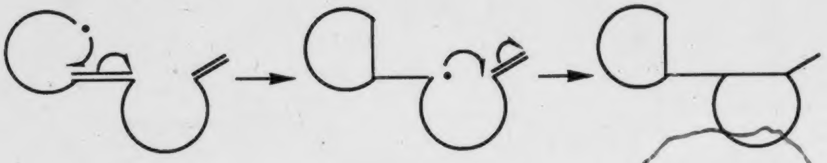
Keck[83] used a slightly different approach to make **76** (eq. 59) which was set up for conversion to **77**, as shown by Stork.[82]



eq. 59

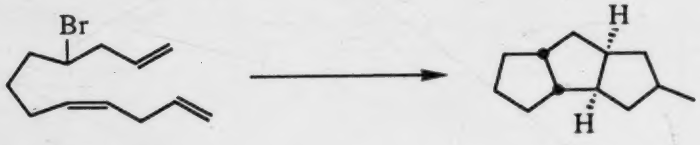
4- Tandem cyclization:

Tandem radical cyclization is a process whereby the alkyl radical cyclizes onto a π-system to generate another radical (eq. 60) which in turn cyclizes onto yet another appropriately located π-system.



eq. 60

Beckwith[84] studied these reactions from a theoretical point of view and found that when **78** was subjected to radical cyclization conditions, it produced predominantly **79** (eq. 61).

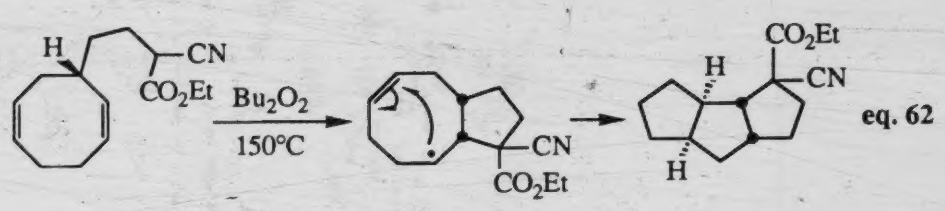


78

79
(major)

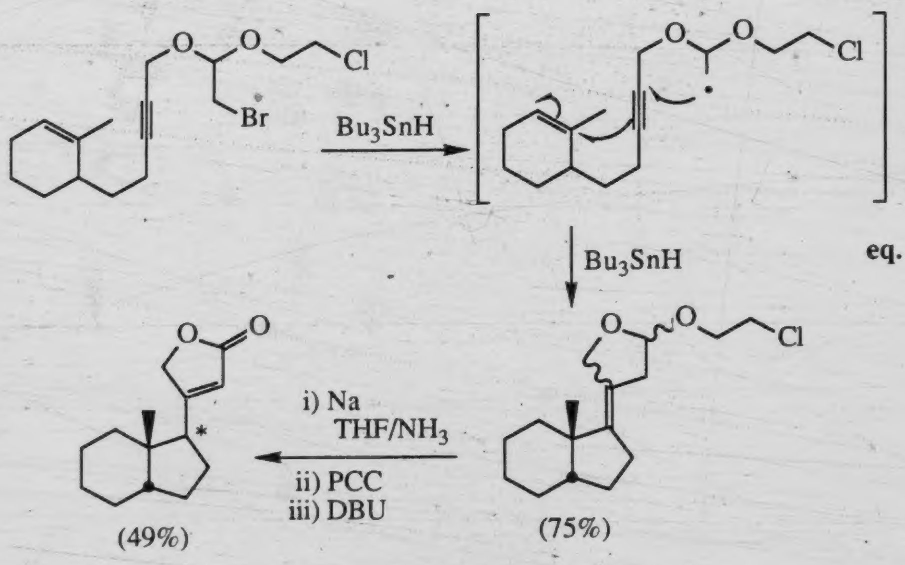
eq. 61

Another example of this methodology was reported by Winkler[85] (eq. 62).



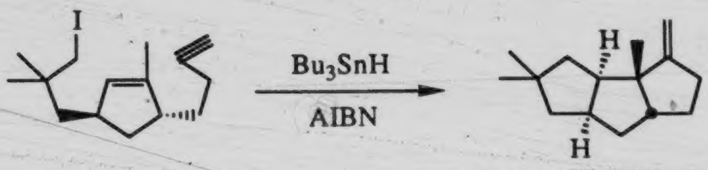
eq. 62

Unsaturated lactones have been synthesized by tandem radical cyclization utilizing both a double and a triple bond[86] (eq.63).



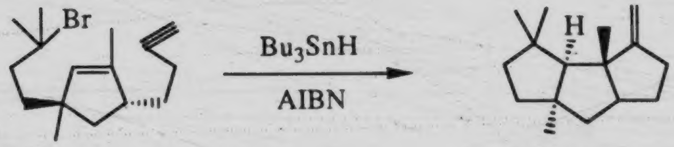
eq. 63

Curran exploited this linear radical cyclization and synthesized a number of natural products. Starting from precursors which were easily assembled, he then subjected them to radical cyclization conditions to produce highly condensed systems. Four examples are illustrated in (eq. 64-67) below.[87-92]



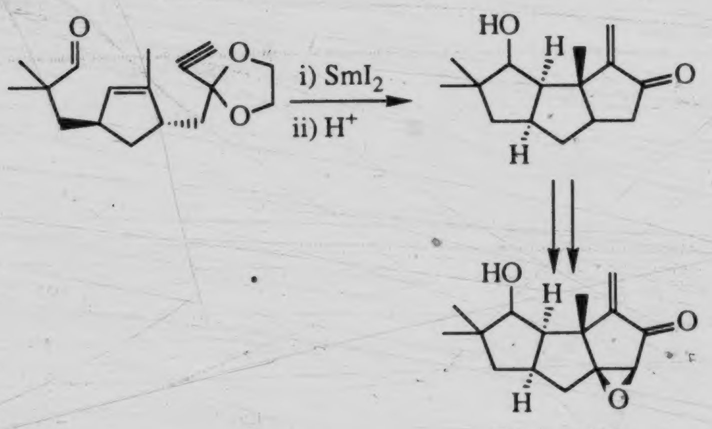
Hirsutene

eq. 64



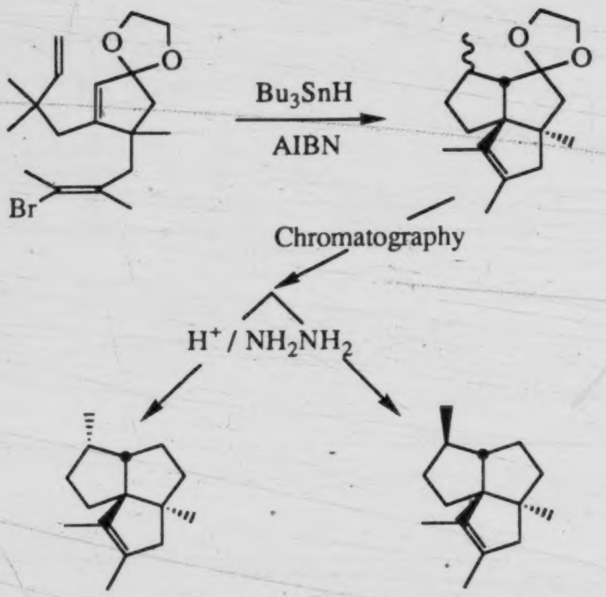
(±)- $\Delta^{9(12)}$-Caplellene

eq. 65



Hypnophilin

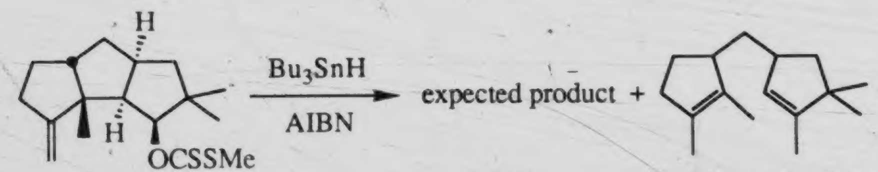
eq. 66



(±)-9-Episilperfolo-6-ene **(±)-silphiperfol-6-ene**

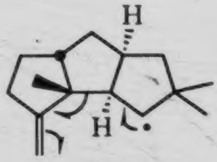
eq. 67

On the other hand, Mehta reported in 1986 that radical ring opening of a 5-membered ring occurred when he tried to reduce **80** (eq. 68).[93] Compound **81** was formed presumably via radical **82**.



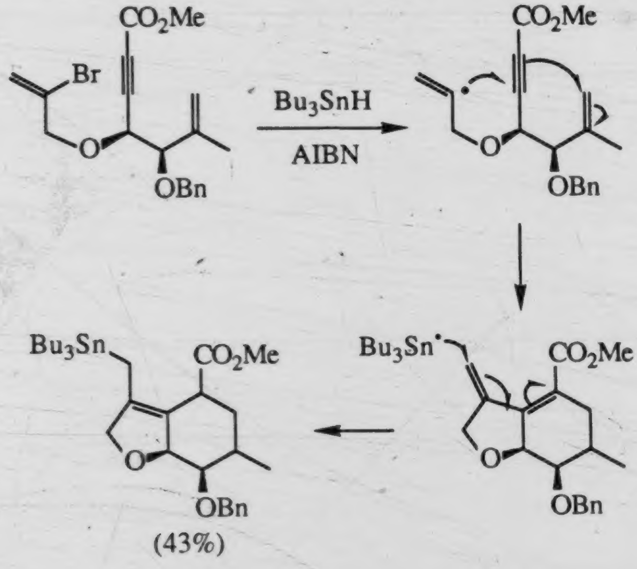
eq. 68

80 (19%) **81** (19%)



82

And finally, an approach towards the synthesis of the lower portion of the insecticide avermectin was reported by Parson[94] using tandem radical cyclization (eq. 69)

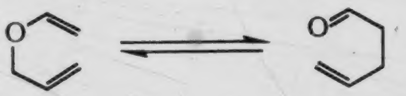


eq. 69

ii) CLAISEN REARRANGEMENT.

After its discovery in 1912,[95] the Claisen rearrangement had to wait half a century to be recognized, in the mid 1960's, as a useful synthetic tool for organic chemists.

The Claisen rearrangement involves the thermal sigmatropic reorganization of an allyl vinyl ether **83** into a homoallylic carbonyl compound **84** (eq. 70) by a concerted intramolecular process.[96]



eq. 70

83 **84**

It can also be looked upon as an intramolecular S_N2' addition of a carbonyl enol to an allylic ether, forming a carbon-carbon σ bond ([3,3] sigmatropic rearrangement) with concomitant double bond migration.[97]

The Claisen rearrangement can be categorized depending on the nature of the vinyl allyl ether[98-104] as shown in (Figure 3).

Not only synthetically but also theoretically, the Claisen rearrangement was well received in the mid 1960's. Woodward has carried out a theoretical evaluation of this reaction.[105]

In the present short overview of the Claisen rearrangement, attention will be focused on the last two classes described below, namely the Johnson orthoester and the Ireland rearrangements as

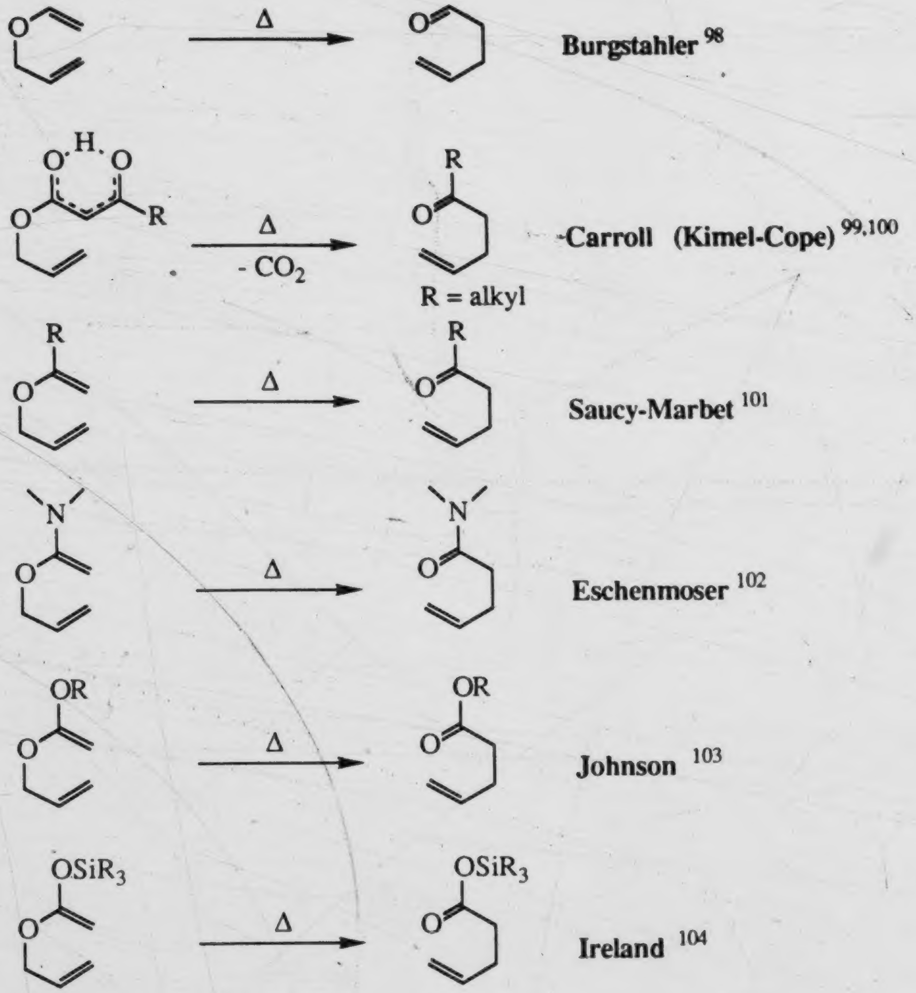
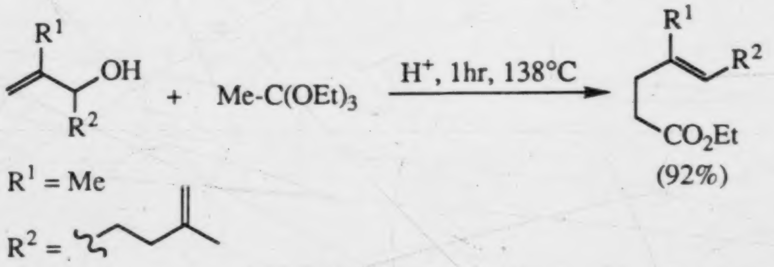


Figure 3. Types of Claisen rearrangement according to the nature of the vinyl allyl system

they are the two types used in the first part of the research discussed for making 5-membered carbocycles with stereocontrol. Also the aza-analogue of the Claisen rearrangement will be discussed briefly as this rearrangement was studied in the course of my research.

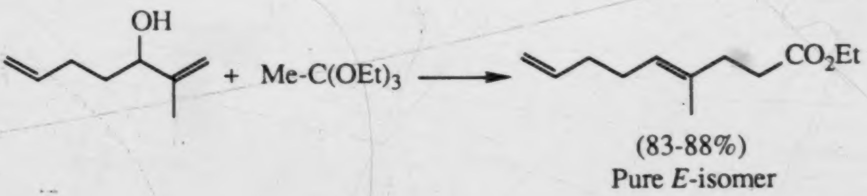
1- ORTHOESTERS IN THE CLAISEN REARRANGEMENT:

The first report using orthoesters[106] in the Claisen rearrangement was by Johnson[107] (eq. 71). He obtained a high level of stereoselectivity and the rearrangement products contained the *trans* olefin.



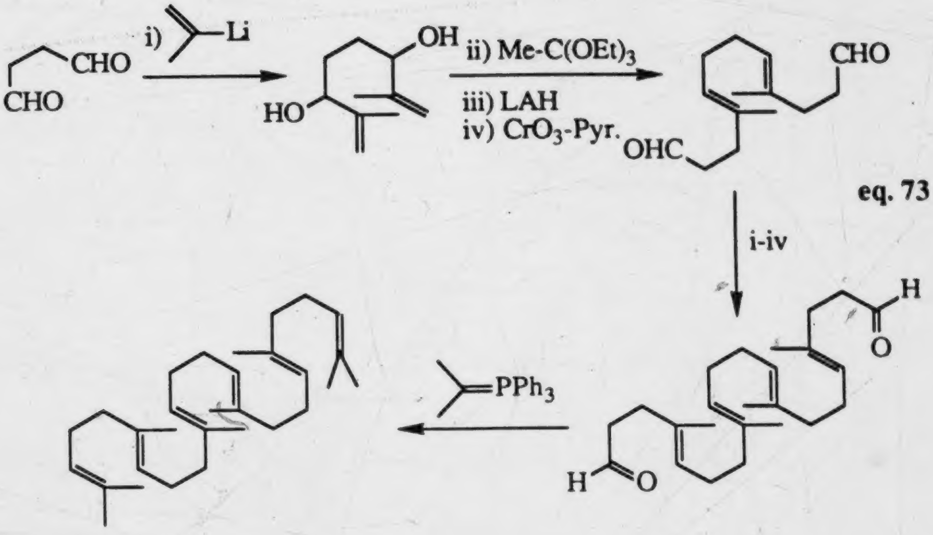
eq. 71

Other workers also reported on the high stereoselectivity of the Claisen rearrangement using orthoesters[108] (eq. 72).



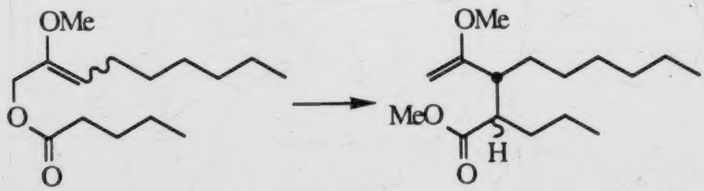
eq. 72

Synthetic application of the Claisen orthoester rearrangement is impressively illustrated in the following routes to squalene[107] (eq. 73).



eq. 73

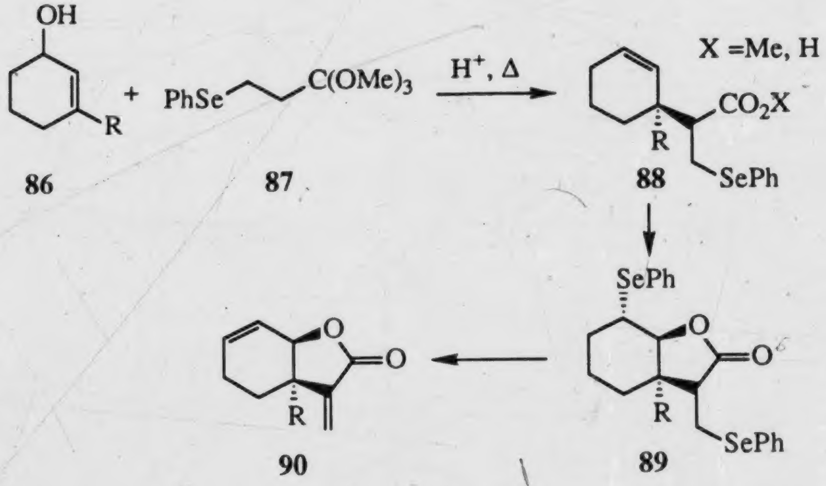
Orthoesters were not only used as reagents to react with allylic alcohols to promote the Claisen rearrangement, but were also used as reagents to trap enolate anions generated from keto esters, prior to the rearrangement of such intermediates[104b,109,110] (eq. 74).



eq. 74 [104b,109]

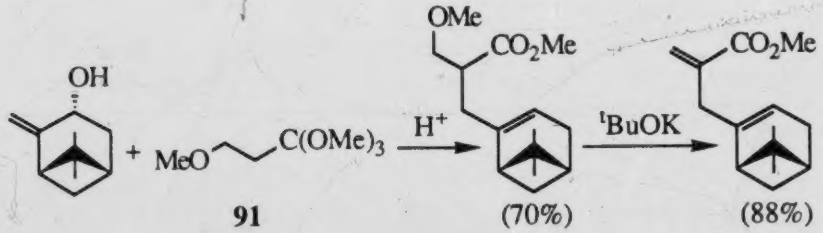
Configuration of starting material	Solvent	product distribution (%) β-H	 α-H
Z	THF	88	12
Z	THF / HMPA	20	80
E	THF	21	79
E	THF / HMPA	85	15

Raucher[111] demonstrated the usefulness of orthoesters as synthons for the preparation of α-methyl-γ-butyrolactones **90** via Claisen rearrangement with allylic alcohols (eq. 75).

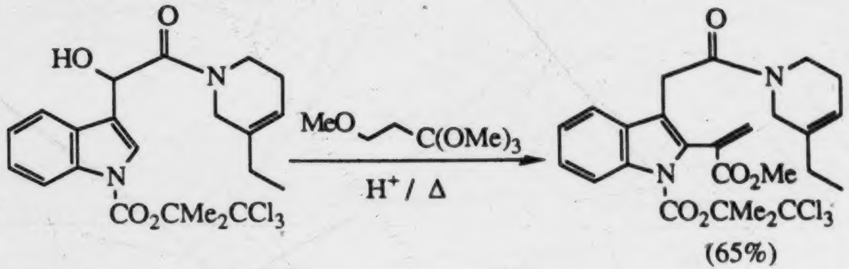


eq. 75

He also utilized the thermally stable β-(methoxy)orthoester **91**, which is stable at 190°C for a prolonged time, for the preparation of methyl α-substituted acrylates via Claisen rearrangement[112, 113] (eq. 76, 77).

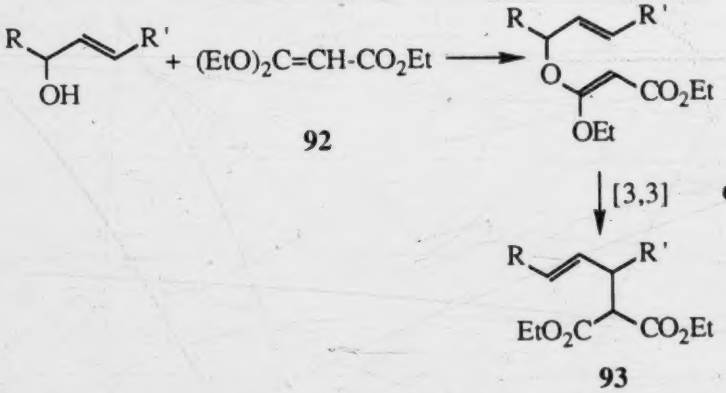


eq. 76[112]



eq. 77 [113]

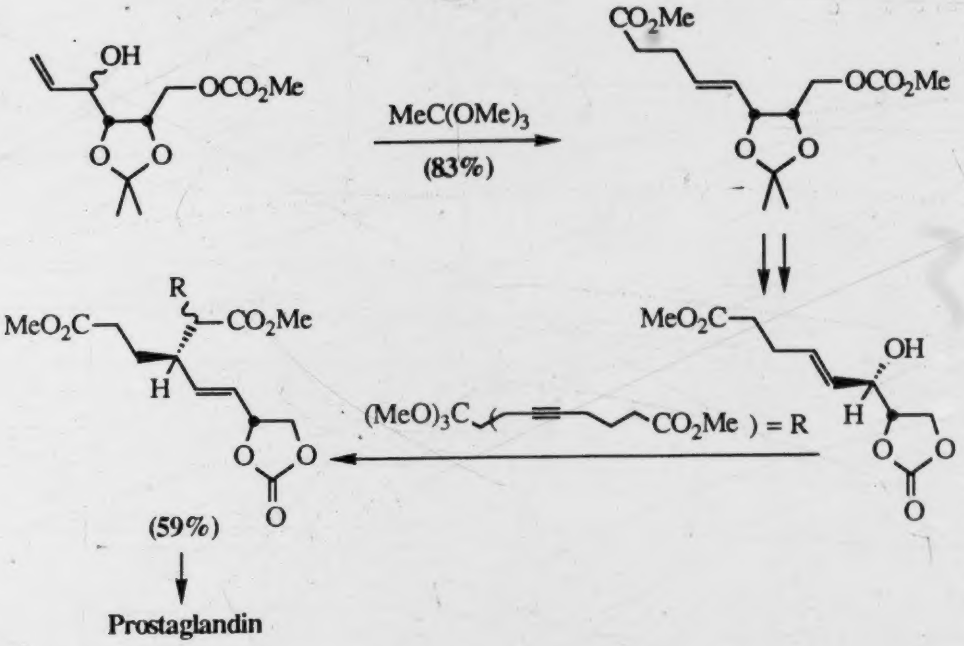
The equivalent of an orthoester, β,β-diethoxyacrylate **92**, was also utilized as a useful synthon in the regiospecific synthesis of substituted allyl malonates **93** in high yield[114] (eq. 78).



eq. 78

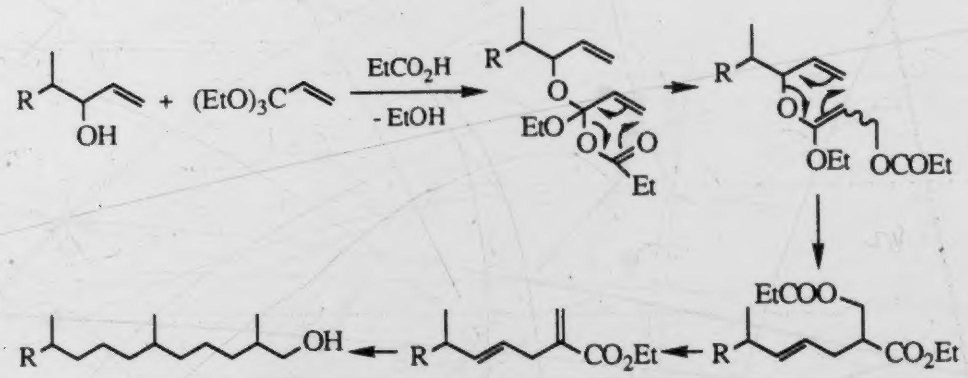
An example of the use of two Claisen orthoester rearrangements in the synthesis of prostaglandin (PGA) was reported by Stork[115] (Scheme 12).

Scheme 12



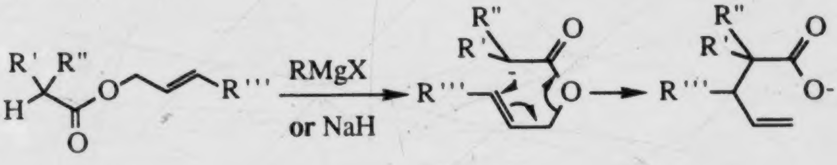
Finally, an allyl orthoester has also been used as a synthon in the Claisen orthoester rearrangement in the presence of excess propionic acid[116] (Scheme 13).[97,98,117]

Scheme 13

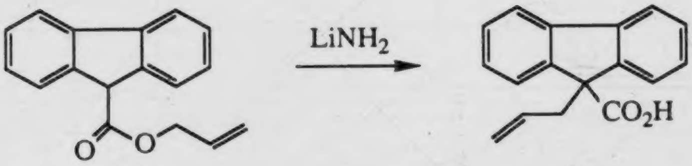


2- ALLYL ESTER ENOLATE REARRANGEMENTS:

Claisen rearrangement involving the enolate anion of an allyl ester has some advantages over the use of orthoesters. It can proceed at lower temperature (< 100°C), and it does not require an excess of reagent. However, the enolate rearrangement is known to lead to acetoacetic ester condensation.[118,119] This condensation can be avoided if one uses an allyl ester of an acid that has only one hydrogen in the α-position (eq. 79, 80).

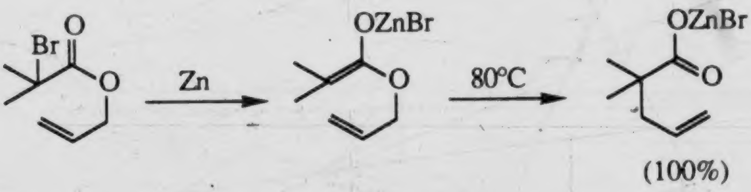


eq. 79 [119a]



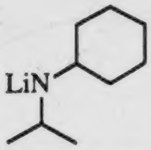
eq. 80 [119b]

Baldwin used the Reformatsky reaction to establish the required intermediate for Claisen rearrangement[120] (eq. 81).



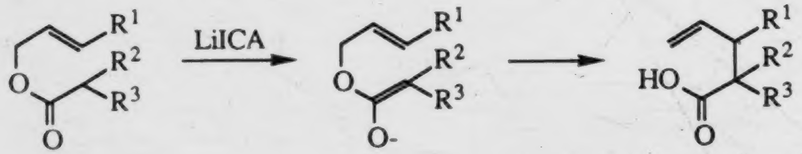
eq. 81

In 1971, Rathke and Lindert[121] found that lithium *N*-isopropylcyclohexylamide (**LiICA**) generated enolates that do not self-condense even at room temperature. This led to a new



LiICA

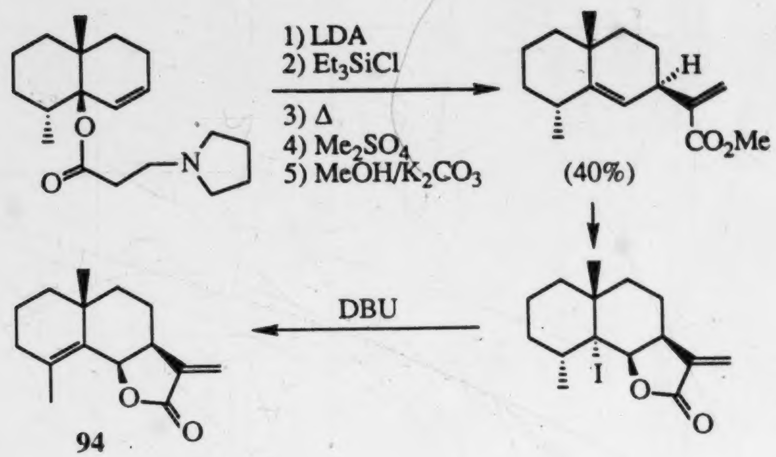
era of Claisen rearrangement. In this evolutionary period of Claisen rearrangement, Ireland[122] found that trapping the enolate anion with TMSCl gave better yields of the product (eq. 82).



eq. 82

good yield when $R^1 = R^2 = Me$
poor yield when $R^1 = R^2 = H$
TMSCl gave better yield regardless of the nature of R's

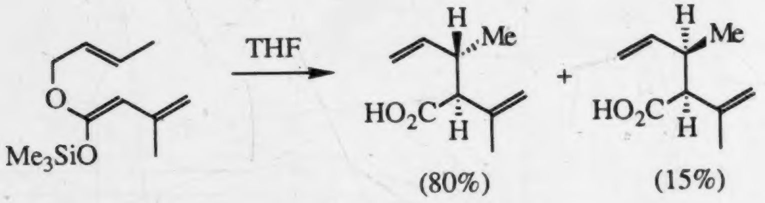
Another example of using trialkylsilylchloride as a trapping reagent is illustrated in eq. 83.[123] In this example an olefinic acrylate was prepared and then converted to the allergenic sesquiterpene frullanolide **94**.



94

eq. 83

These trapped enolates (silylketene acetals) were found to undergo the rearrangement at low temperatures with high stereoselectivity[124-126] (eq. 84).



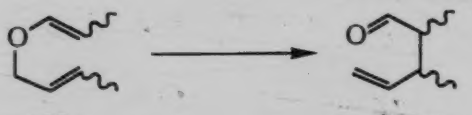
eq. 84 [124]

3- STEREOCHEMISTRY OF CLAISEN INTERMEDIATES AND TRANSITION STATES:

The powerful stereochemical control afforded by the Claisen rearrangement in the construction of cyclic systems has been recognized[97,98,127] especially since the development of methods for producing either *Z* or *E* ketene acetals.[102,128,129]

The high stereoselectivity of the Claisen rearrangement is attributed to the geometry of the enolate as well as the conformation of the transition state.

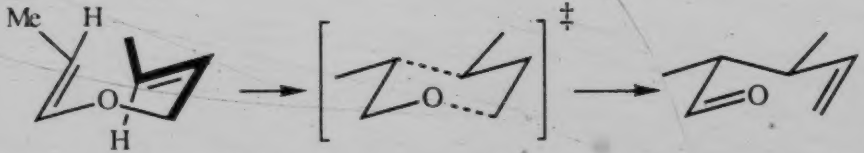
It was pointed out in a typical Claisen rearrangement (**95** → **96**) (eq. 85) that the rearrangement proceeds through a chair-like



95 **96**

eq. 85

transition state rather than through a boat-like transition state[129] (eq. 86).

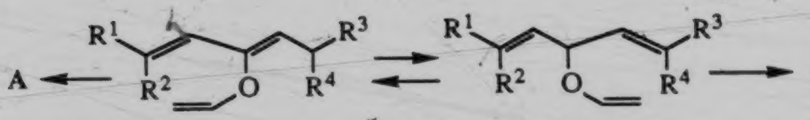


trans geometry preferred

eq. 86

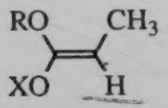
A competition reaction was carried out to prove this claim as shown in (eq. 87).

In 1976, Ireland[129] reported that the geometry of the enolate is solvent dependent. A *Z* geometry is preferred if the solvent is THF; however, in a THF/HMPA solvent, the *E* enolate is preferred.

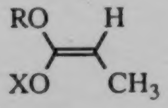


eq. 87

Substrate	%A	%B
$R^3 = CH_3$ $R^1 = R^2 = R^4 = H$	66	33
$R^4 = CH_3$ $R^1 = R^2 = R^3 = H$	95	5
$R^1 = R^4 = CH_3$ $R^2 = R^3 = H$	78	22
$R^3 = R^4 = CH_3$ $R^1 = R^2 = H$	100	0



Z if X=Li
THF only



E if X=Li
THF/HMPA

X = Li, $^tBuMe_2Si^*$

This difference can be understood by examining transition states **C** and **D**. When the solvent is the less coordinating THF the interaction of the carbonyl oxygen becomes effectively bulkier than OR'. The resulting nonbonding interactions would bestow a higher activation energy on transition state **D** and enolization would be expected to proceed through transition state **C**. The presence of HMPA, on the other hand, should result in a greater degree of solvation of the lithium cation and an enhanced reactivity of the

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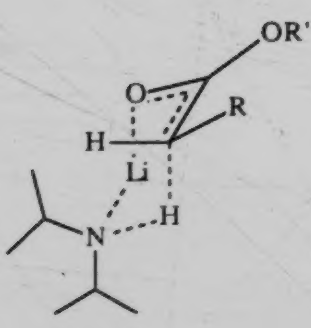
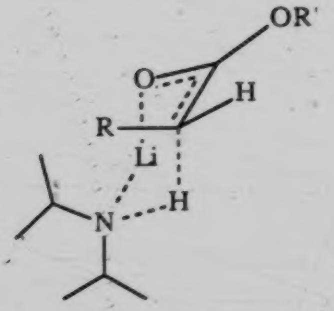
* Note stereochemical descriptions are reversed if X=Si, i.e. the *Z* lithium enolate (without change of geometry) affords the *E* silyl ketene acetal.



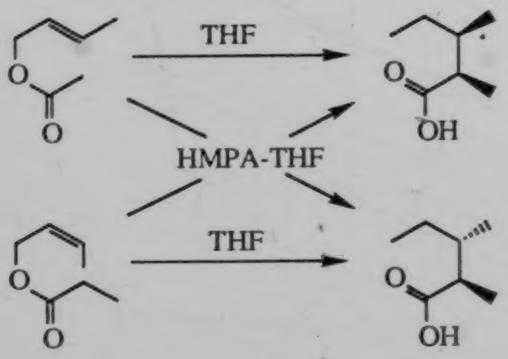
C
THF only



D
THF/HMPA

amide base. The lithium-carbonyl oxygen interaction should be much weaker and transition state **D**, in which R becomes eclipsed with the now sterically smaller carbonyl oxygen during enolization, should be favored.[129,131]

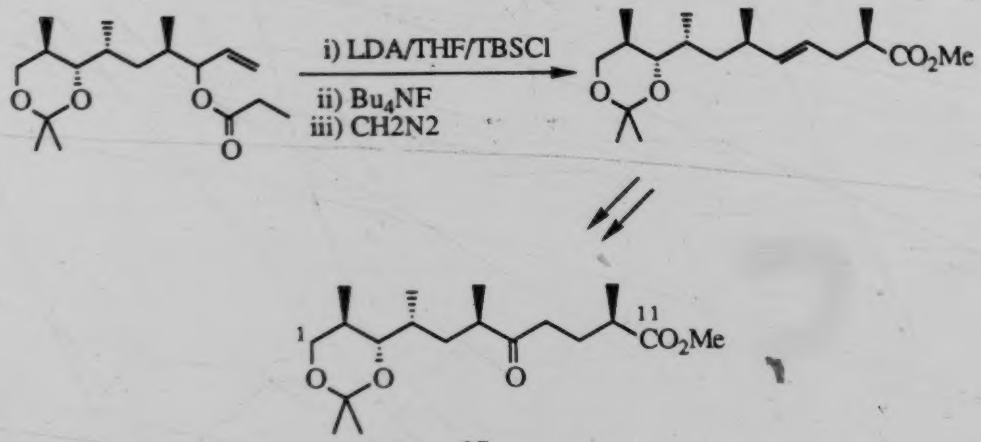
This was demonstrated by the experiments shown in (eq. 88).



eq. 88

This powerful rearrangement was used extensively in a wide range of synthetic problems. The C(1)-C(11) segment **97** of antibiotic X-537A (lasalocide A[132]) was synthesized using this rearrangement[133] (Scheme 14).

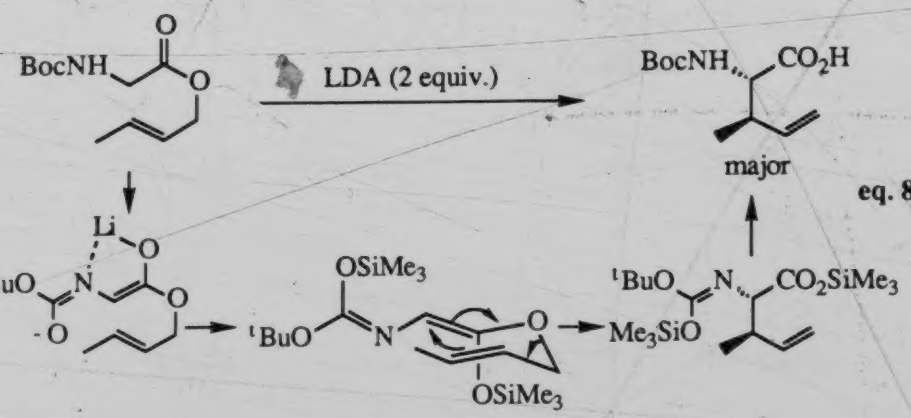
Scheme 14



97

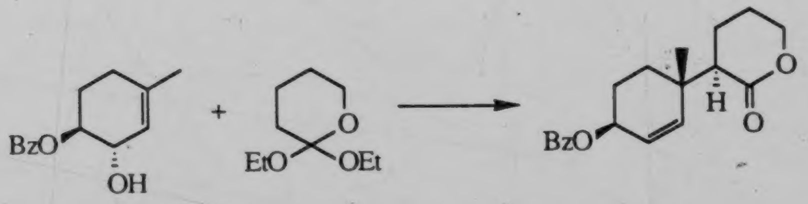
Other polyether antibiotics were also synthesized by this method.[134]

Bartlett[135] showed that allylic esters of *N*-acyl α-amino acids underwent Ireland rearrangement. In this case the *E* enolate was predominate instead of the *Z* enolate under the standard conditions (eq. 89). The reason for the reversal is that the lithium ion coordinates to the nitrogen atom and the carbonyl-oxygen forcing the enolate geometry to be *E*.



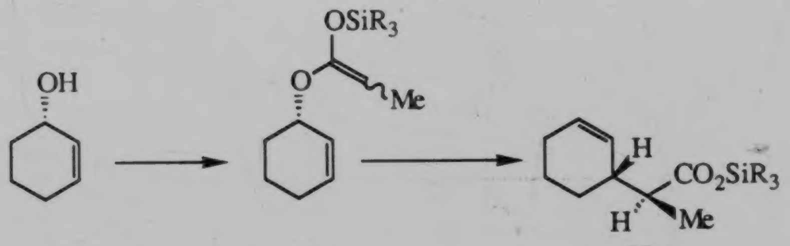
eq. 89

In 1975, Lythgoe and Metcalfe[136] reported a Claisen rearrangement via a boat-like transition state (eq. 90).



eq. 90

Another surprising result was obtained when it was found that either geometry of **98** gave **99** as the major product[137] (eq. 91).

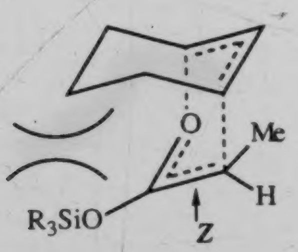


eq. 91

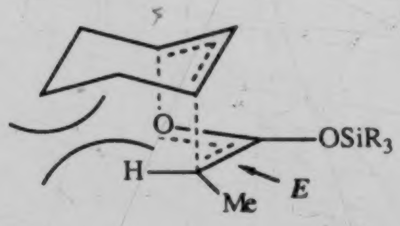
98
either geometry

99
major

The reason for such results can be understood by examining the transition states (**E** and **F**) of the rearrangement. When the



"E"



"F"

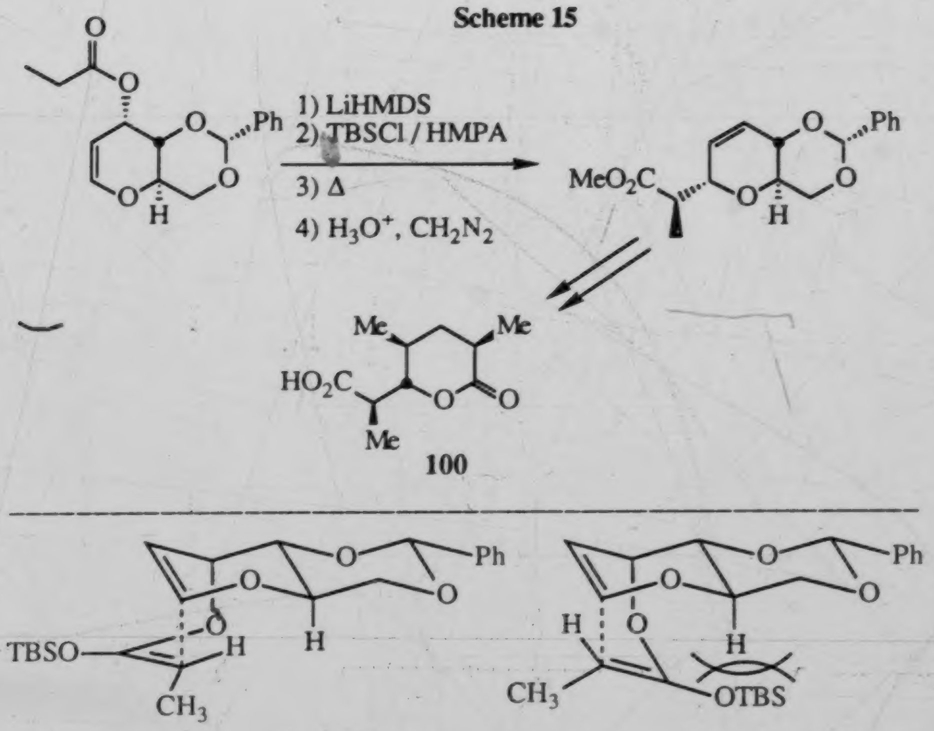
geometry of the enolate is *Z*, the chair-like transition state **E** is favored; on the other hand when the geometry of the enolate is *E*, the boat-like transition state **F** is favored.

This observation is the first example of Claisen rearrangement where the transition state conformation reverses upon the reversal of the enol double bond stereochemistry.

At about the same time, Ireland reported a boat-like transition state in the synthesis of the Prelog-Djerassi lactone **100**, a chiral subunit for macrolide synthesis[138] (Scheme 15).

The reason for the boat-like transition state is due to unfavorable steric interactions in the chair-like transition state (see transition states below):

Scheme 15



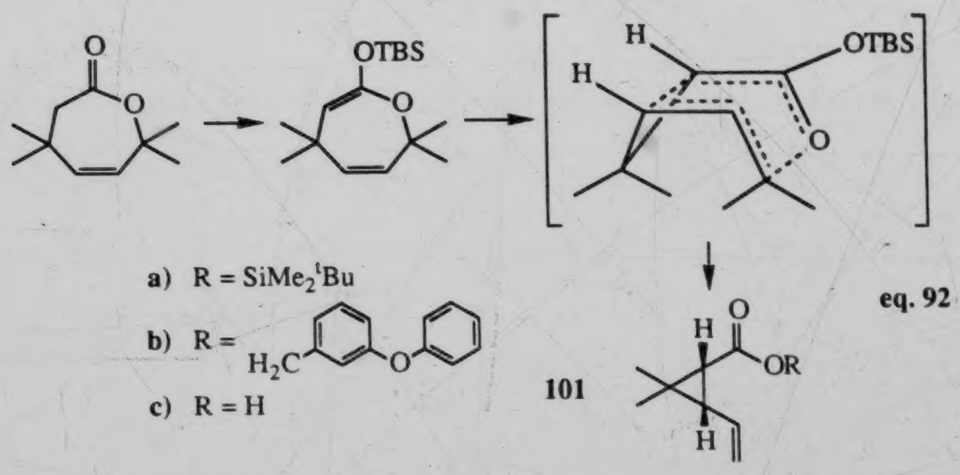
100

boat (**G**)

chair (**H**) destabalized

Other examples of a boat-like transition state can also be found in the literature.[139,140]

Finally, Funk and Munger reported[141] a Claisen rearrangement mediated ring contraction of a macrocyclic ketone acetal. The process was used to make the insecticides of the pyrethroid class, eg.**101b**. The Claisen process involved a boat-like transition state only (eq. 92).



a) R = $SiMe_2{}^tBu$

b) R =

c) R = H

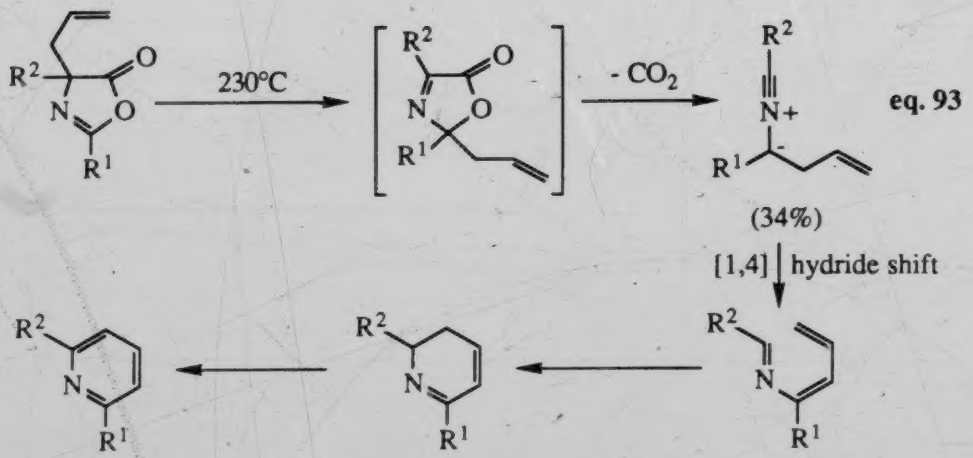
101

eq. 92

In general, Claisen rearrangement of acyclic systems take place via a chair-like transition state.[142,98,97] On the other hand, some boat-like transition states have been detected and they are confined to cyclic systems.[136-138,139a-c,140]

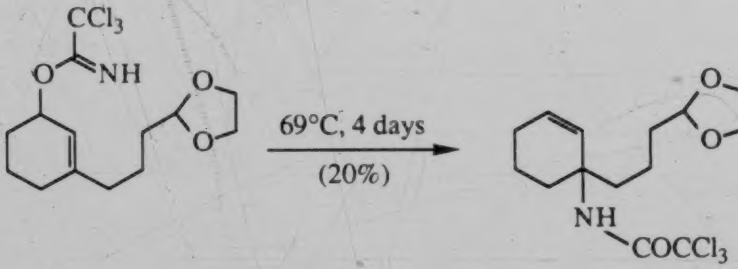
4- AZA CLAISEN:

The early work on this type of Claisen rearrangement has been reviewed.[143,144] It has been estimated that the nitrogen Claisen rearrangement involves an activation energy of about 25 KJ/mol (6 kcal/mol) higher than that of the oxygen analogue.[145] Hence, higher temperatures are needed to drive forward the rearrangement (around 200°C). An example of such a rearrangement is illustrated in (eq. 93) below[146]:



eq. 93

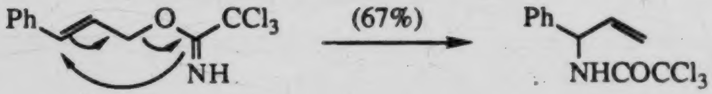
However, an imidate-amide conversion can take place at a much lower temperature[147] (eq. 94).



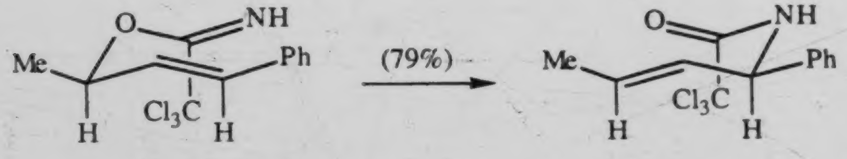
eq. 94

The first report of this kind of conversion was described by Moller in 1937.[148]

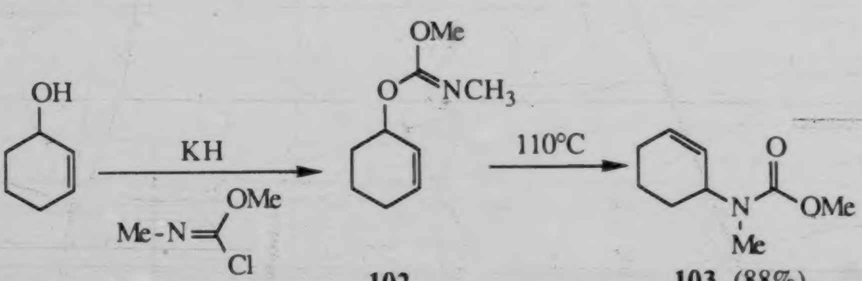
The trichloroacetimide esters[147a-b,149,150] are preferred intermediates for this kind of transformation (eq. 95) as the electron withdrawing nature of the CCl_3- group lowers the energy of the transition state. Also it has been reported by Beak[151] that these transformations are exothermic.


eq. 95

The transfer of chirality in these reactions was demonstrated by Inouye[152] in the rearrangement of (*R*)-3-phenyl-2(*E*)-buten-1-yl trichloroacetimide in a suprafacial manner with complete (>97%) transfer of chirality (eq. 96).


eq. 96

Imidates of type **102** were also used as intermediates for this kind of transformation giving, in the example shown, *N*-allyl carbamate **103**[153] (eq. 97).

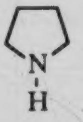

102

103 (88%)

eq. 97

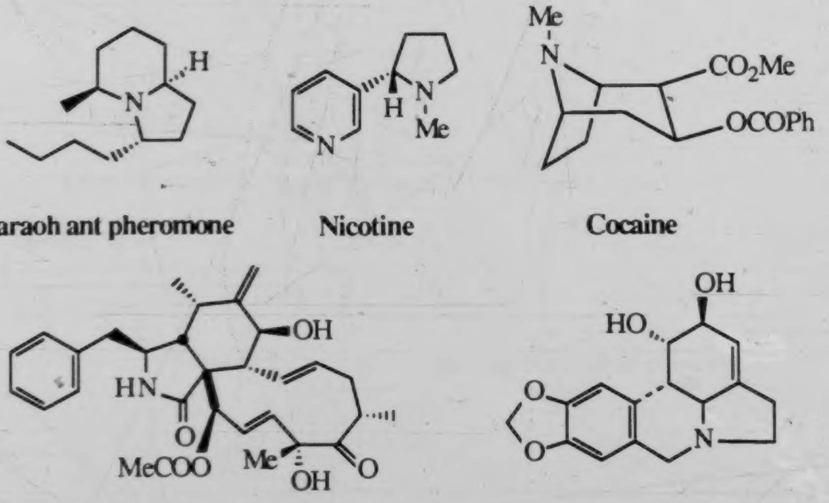
iii) SYNTHESIS OF PYRROLIDINE AND DIHYDROPYRROLE:

Pyrrolidine **105** is a heterocyclic system that appears in



105

many natural products (Figure 4) as a substructural unit and the synthesis of such systems has attracted much attention.



Pharaoh ant pheromone

Nicotine

Cocaine

Cytochalasin D
(fungal metabolite)

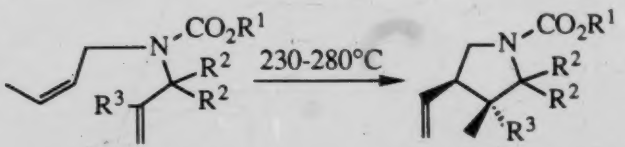
Lycorine

Figure 4. Some natural products that contain the pyrrolidine system

Five general methods for making these systems will be reviewed.

1 - ENE-STRATEGY:

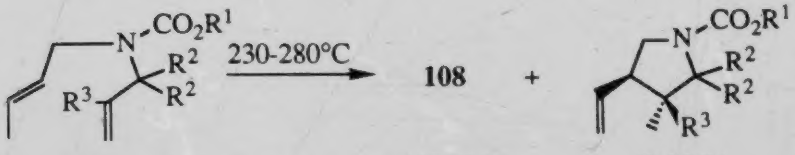
N-Allyl-*N*-(2-butyl)amides **106** have been found to undergo intramolecular ene reaction in a totally regioselective fashion upon heating to a high (>230°C) temperature[154] (eq. 98).



106 **108** (Only product)

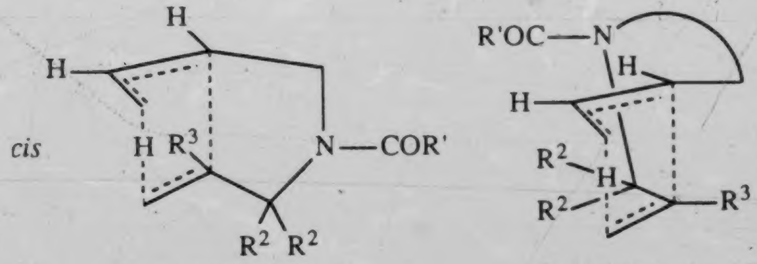
R^1 = Me, OMe
R^2 = H, Me
R^3 = Me, Ph

eq. 98



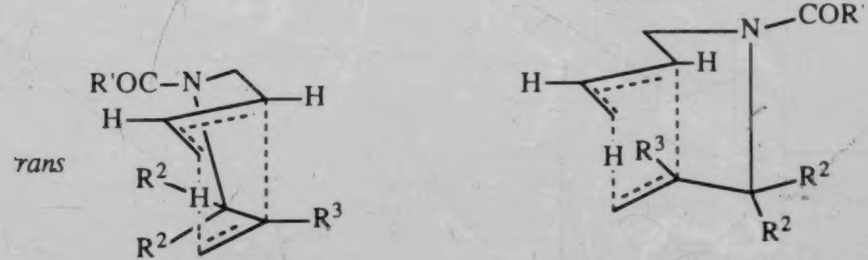
107 (47-71%) (0-23%)

eq. 99



I unstrained TS

J highly strained TS
Disfavored



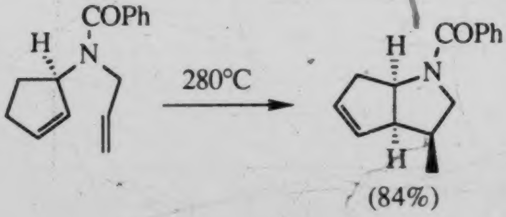
K more favored TS
(R^3 eclipses with H)

L less favored TS
(R^3 eclipses with CH_2)

Transition states for the thermal cyclization of dienes **106** and **107**

The reason why the *trans* isomer **107** (eq. 99) gives two isomeric products can be seen when the transition states (**I**-**L**) are examined. In the cyclization of the *cis* diene **106**, the *endo* transition state **J** appears to be highly strained thus favoring the exclusive formation of the *cis*- substituted pyrrolidine **108** via relatively unstrained *exo* transition state **I**. On the other hand, in the cyclization of the *trans* diene **107**, preference of the *endo* transition state **K** over the *exo* transition state **L** is indicated.

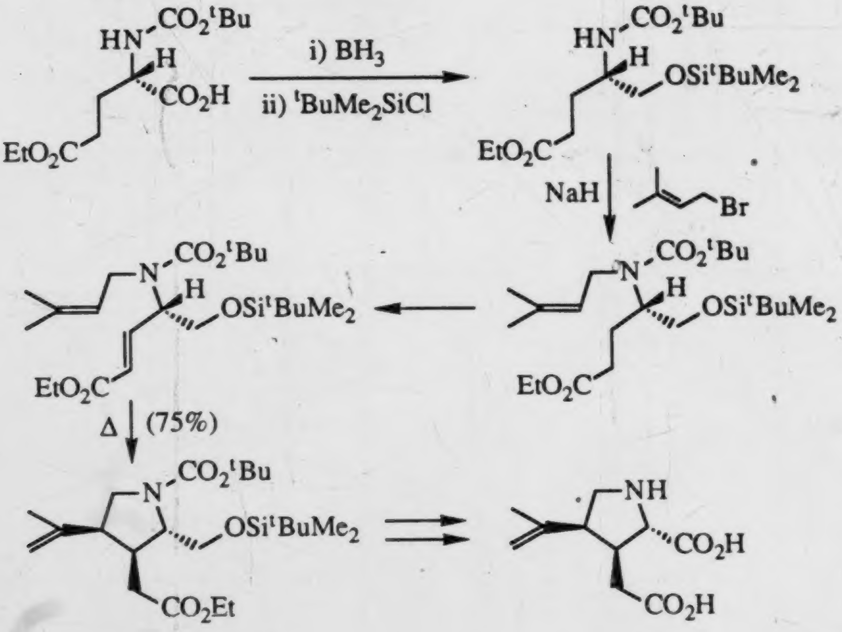
Another example of these ene-reactions is shown in (eq. 100)



eq. 100

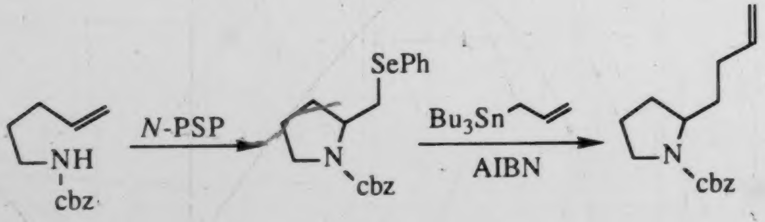
and an application in the synthesis of the natural product α-kainic acid,[155,156] is shown in Scheme 16.

Scheme 16

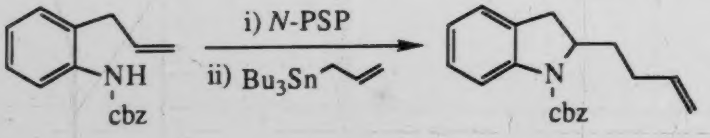


2 - ELECTROPHILE PROMOTED CYCLIZATION OF UNSATURATED AMINE DERIVATIVES:

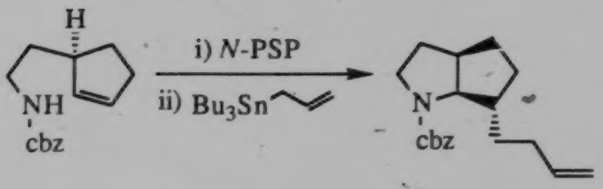
a) Intramolecular ureidoselenenylation of a double bond followed by allylative deselenenylation accomplishes a net ureidoallylation.[157]. Typical examples are given in eq. 101-103:



eq. 101

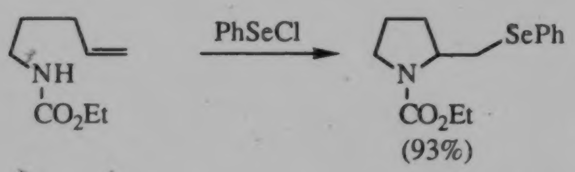


eq. 102

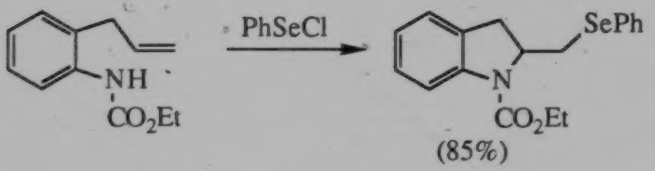


eq. 103

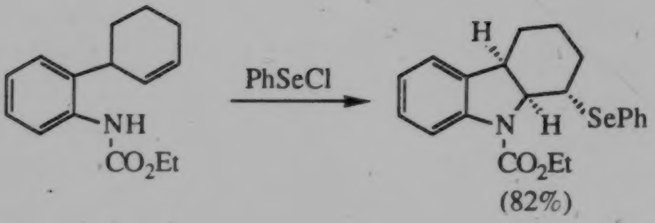
b) The above work was modelled on earlier results of Clive,[158] who had developed an electrophile promoted cyclization of amide esters using PhSeCl (eq. 104-106).



eq. 104

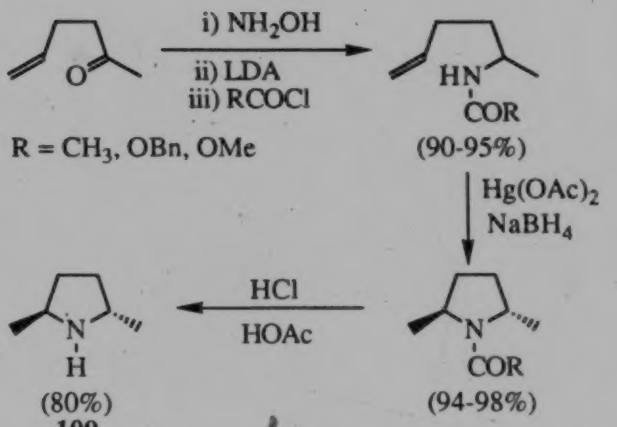


eq. 105



eq. 106

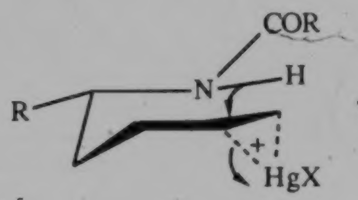
c) δ-Alkenyl amine derivatives also undergo stereoselective mercury-initiated cyclization[159]. For example, preparation of the chiral *trans*-2,5-dimethylpyrrolidine **109**, which has a C_2 axis of symmetry, can be accomplished by this method (eq. 107).



eq. 107

109

The reason for the observed *trans* geometry lies in the preferred orientation of the transition state below:

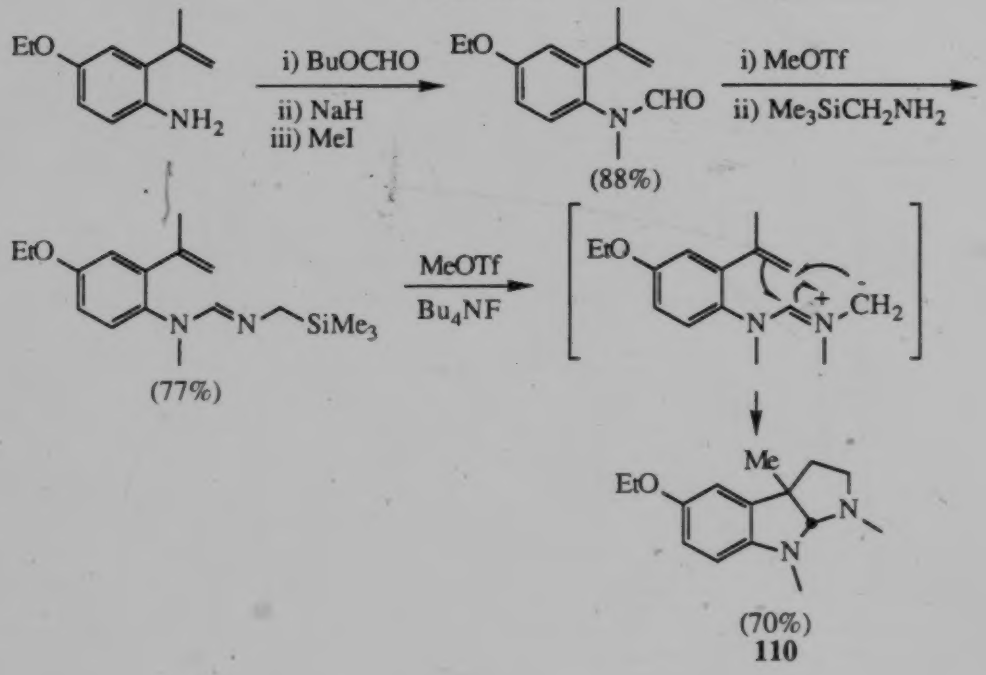


Transition state

3 - 1,3-DIPOLAR CYCLIZATION METHOD:

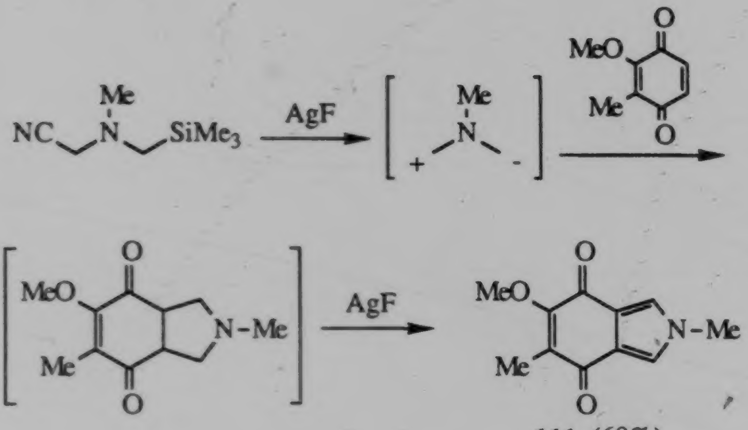
Several examples for making pyrrolidine systems have been reported in the last few years using the 1,3-dipolar cyclization approach. The only difference between these examples is primarily the method used to generate the dipolar intermediate that will eventually yield the pyrrolidine ring. In 1983, Smith[160] reported the first example of an intramolecular dipolar cyclization of a formamidine ylide, generated from a silane, to an unactivated

Scheme 17



olefin. The utility of this reaction was demonstrated by making the natural product eserethole **110** as shown in Scheme 17.

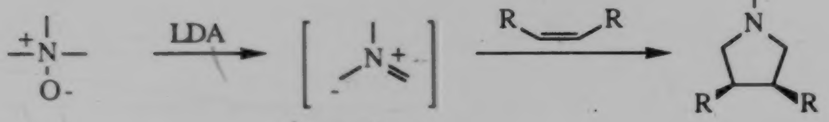
Silanes were also used by Parker[161] in 1984 to generate the 1,3-dipolar moiety that then undergoes cyclization. This method was applied to synthesize isoindole **111** (eq. 108), which is an active agent against Staphylococcus aureus, Bacillus subtilis, Vibrio anguilarium and B-392, a marine pseudomonal.



111 (68%)

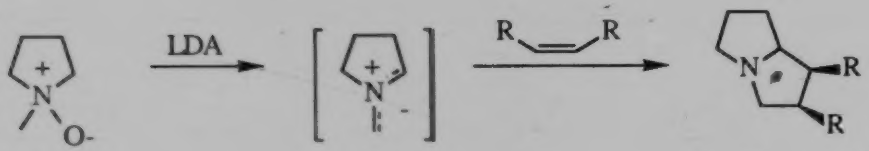
eq. 108

Unactivated double bonds also reacted with the highly reactive, non stabilized ylides **112a,b** (eq. 109, 110) that were generated from an *N*-oxide and LDA.[162]



112a

eq. 109

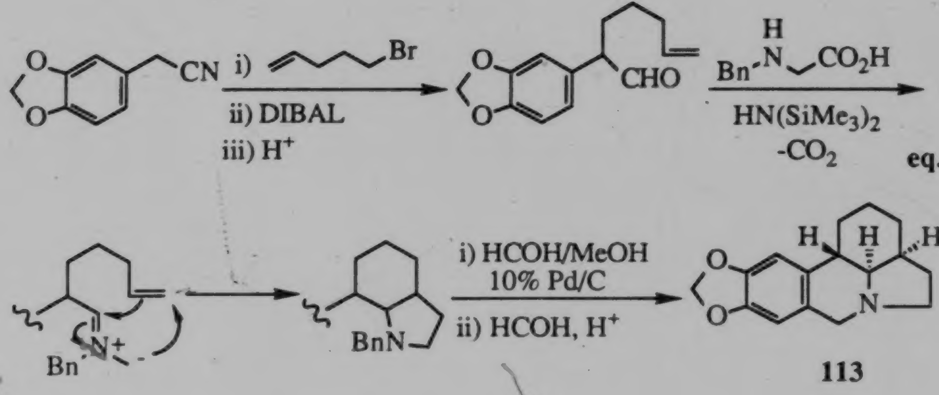


112b

R = Ph (43%)
R = $(CH_2)_3$ (79%)

eq. 110

A stereospecific synthesis of (±)-α-lycoran **113** in 5 steps (eq. 111) was reported using this cyclization approach.[163,164]



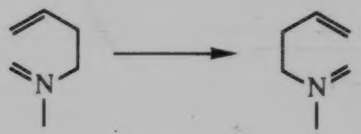
eq. 111

113

There are further methods[165,166] for making these 1,3-dipolar moieties.

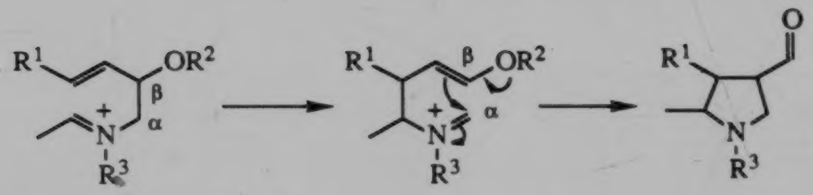
4 - TANDEM CATIONIC AZA-COPE REARRANGEMENT-MANNICH REACTION SYNTHESIS:

This kind of work was extensively explored by Overmann.[167-169] The aza-Cope rearrangement shown below is a 2-azonia [3,3]-sigmatropic rearrangement.[170]

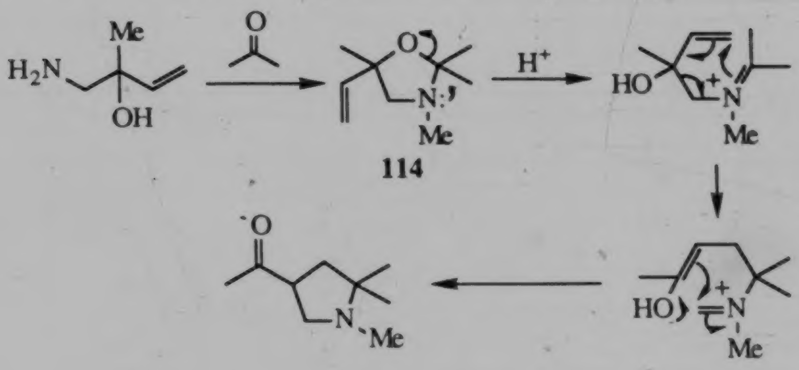


aza-Cope rearrangement

If an alkoxy group is present at the β-position (eq. 112), the rearrangement would be followed by a Mannich reaction and formation of the pyrrolidine ring.



eq. 112

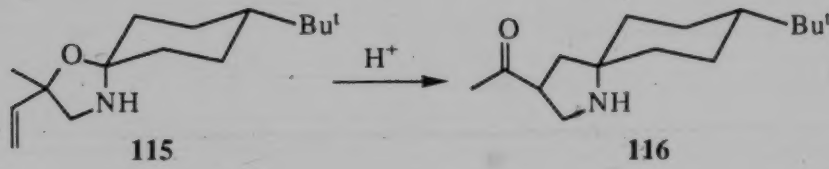


114

eq. 113

In this way system **114** led (eq. 113) to the pyrrolidine shown.

Spiro pyrrolidines, eg. **116**, are also available by this method[169] (eq. 114).



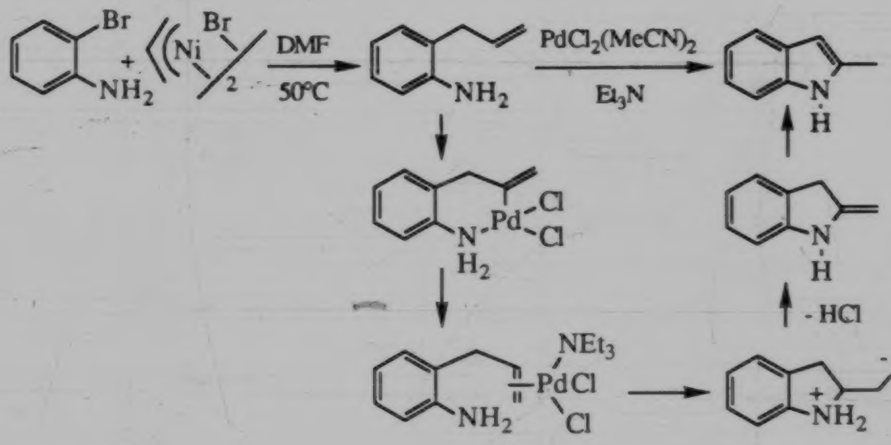
115

116

eq. 114

5 - TRANSITION METAL CATALYZED CYCLIZATION OF UNSATURATED AMINES:

2-Bromoanilines were converted to 2-allylanilines by treatment with π-allylnickel halide complex (eq. 115). Treatment of these allyl anilines with palladium chloride then afforded 2-methylindoles or quinolines.[171]

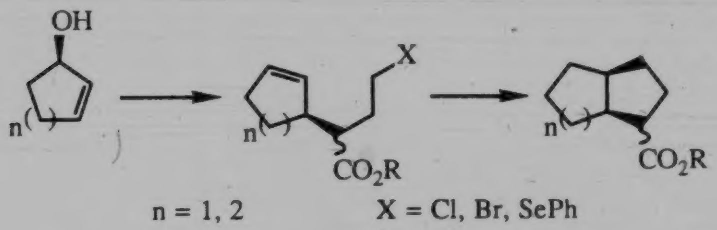


eq. 115

(II) DISCUSSION

i) PREPARATION OF CARBOCYCLES:

In the ongoing efforts in our laboratory to construct carbocycles via radical cyclization methodology,[30,32,35,36,77] easy and general routes to the substrates are needed. For a method to be of synthetic value, the stereochemistry throughout must be controlled and predictable. As part of our work, we envisioned the conversion of allylic alcohols to 5-membered carbocycles via the Claisen rearrangement[111] (eq. 116).

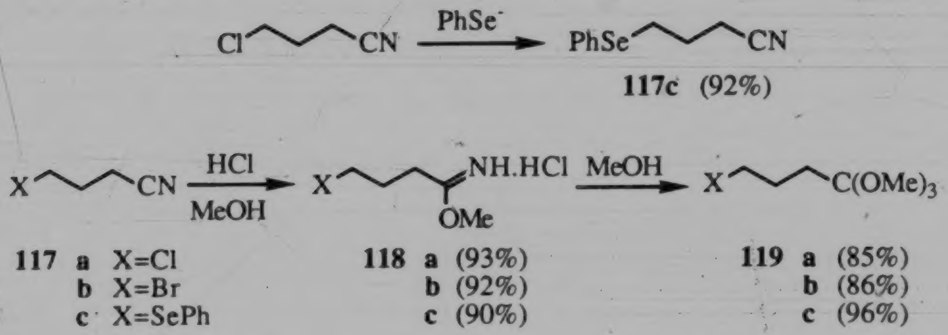


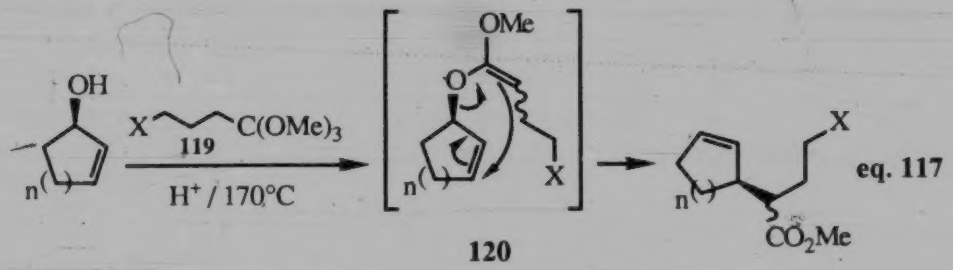
eq. 116

Our first approach to the Claisen rearrangement was the use of orthoesters **119** as Claisen reagents. These orthoesters were made (Table 1), by the Pinner reaction, from the corresponding nitriles **117**. For example, nitrile **117a** was treated with dry HCl and one equivalent of dry methanol in ether at -20°C to afford the corresponding imidate hydrochloride **118a** in good yield. Orthoester **119a** was then formed in high yield by the treatment of **118a** with two more equivalents of dry methanol in hexane at room temperature.

To carry out the Claisen rearrangement, cyclic allylic alcohols were reacted (eq. 117) with orthoesters **119** in the presence of

Table 1. Preparation of orthoesters 119a-c



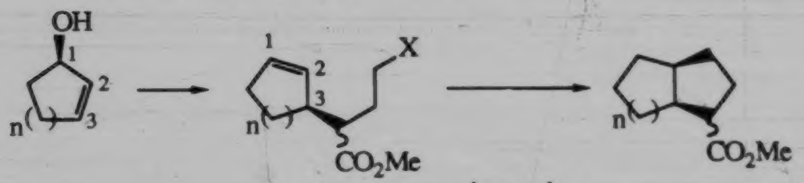


120

n = 1, 2, 3 X = Cl, Br, SePh

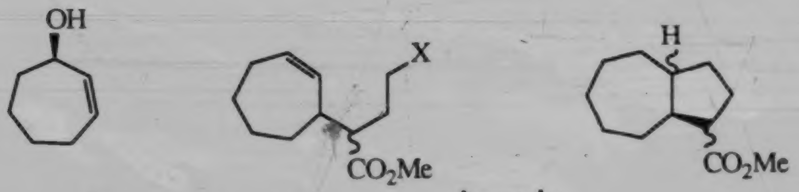
trimethylacetic acid as a catalyst to afford ketene acetals **120**. These ketene acetals underwent Claisen rearrangement under the reaction conditions to produce the corresponding rearranged esters **122**, **125**, and **128**.

Table 2. Synthesis of carbocycles using orthoesters as Claisen reagents



					isomeric ratio			
121 (n=1)	**122**	**a**	X=Cl	(80%)	(40:60)	**123**	-------*	from **122 a**
		b	X=Br	(25%)	-----		-------*	from **122 b**
		c	X=SePh	(41%)	(50:50)		(70%)	from **122 c**

					isomeric ratio			
124 (n=2)	**125**	**a**	X=Cl	(47%)	(40:60)	**126**	(62%)	from **125 a**
		b	X=Br	(29%)	-----		-------*	from **125 b**
		c	X=SePh	(40%)	(70:30)		(47%)	from **125 c**



					isomeric ratio			
127	**128**	**a**	X=Cl	(87%)	(36:64)	**129**	(43%)	from **128 a**
		b	X=Br	(79%)	**		(76%)	from **128 b**
		c	X=SePh	(30%)	**		(78%)	from **128 c**

All yields quoted are of purified products.

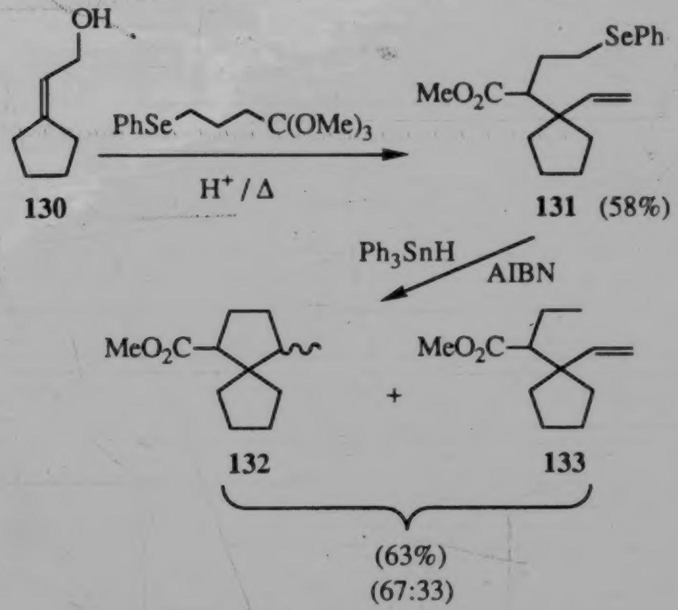
* Experiment was not carried out.

** The methoxy signal in the ^{1}H NMR appeared as one broad signal

The esters were cyclized by using Ph$_3$SnH to give the corresponding bicyclic systems (Table 2). As can be seen, there was a transfer of chirality (see first example, Table 2) from C(1) in **121** to C(3) in **122**. We did not use optically active allylic alcohols in our experiments, but use of an alcohol of known stereochemistry, say with absolute stereochemistry **121**, then the pendant in the Claisen rearrangement will be transferred suprafacially as shown in eq. 117 to generate a new chiral centre at C-3. The other stereochemical feature of this methodology, concerns the ring fusion geometry of the cyclized products, and will be discussed later.

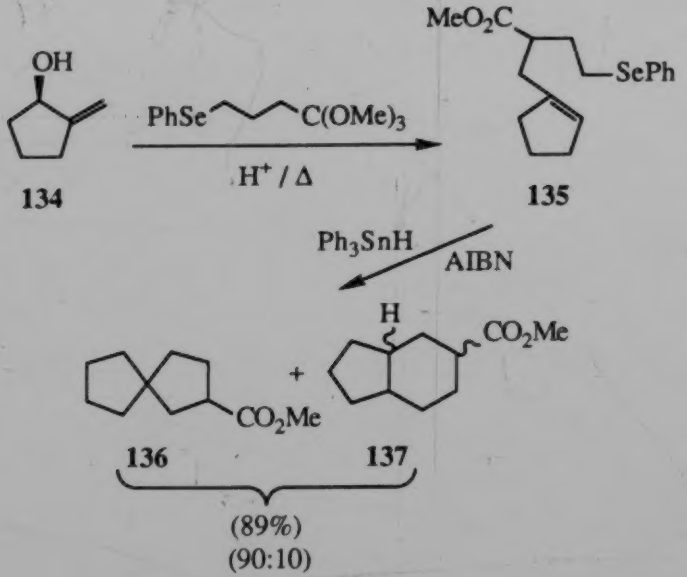
The yields of the rearrangement step (Table 2) were variable. In some cases, e.g. **122a** and **128a**, we were able to obtain very high yields; however, in other cases, e.g. **122b** and **125b**, the yields were quiet low.

In the cyclization step, we obtained generally good yields when starting with bromo- or (phenylseleno)- esters, e.g. **122b** and **128c** (Table 2). The other feature worth noting about Table 2 is the cyclization of chloro esters, eg. **128a** → **129**. Chloro esters are known to react slowly with tin hydrides.[172] The reason for such behavior is that the propagation step in the radical chain mechanism is slow, a fact which then permits side reactions to take place. In the other cases, i.e. the bromo- and (phenylseleno)-esters, the propagation step is faster than any side reaction. Therefore, to speed up the propagation step in the cyclization of chloro esters, one must use higher concentrations of the tin hydride reagent. However, this is not desirable in our case as we want to give the free radical generated by the cleavage of the C-Cl bond enough time to cyclize onto the intramolecular double bond. Having high concentration of the tin hydride reagent will lead to the trapping of the radical before cyclization takes place and hence defeat the purpose of our experiment. Therefore we focused our attention on phenylseleno esters. We also attempted the conversion of allylic alcohol **130**[173] to the spiro compound **132** (eq. 118). In this attempt, however, when subjecting the rearranged product **131** to our radical cyclization conditions, we observed the desired compound **132** as well as some reduction product **133**. The ratio of **132** to **133** was about 2:1. This relatively high amount of reduction product is not seen in any other cyclizations and no explanation is available.



eq. 118

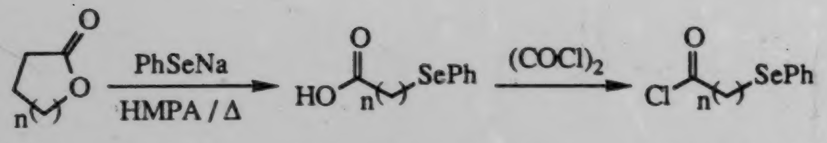
A second route for making spiro carbocycles is illustrated in eq. 119. Allylic alcohol **134** was converted to ester **135** as described above. When **135** was treated with triphenyltin hydride to effect radical ring closure, compound **137** was produced in low yield via a 6-*endo* closure pathway. This was expected[16,174,175] as C(1) of the cyclopentenyl unit is a tertiary center.



eq. 119

As can be seen from the above discussion, the conversion of cyclic allylic alcohols to the corresponding Claisen rearranged products was proceeding in about 25-87% yield and a better method for this kind of conversion was needed. Therefore, we shifted our attention to the Ireland rearrangement which gave us greatly improved results.

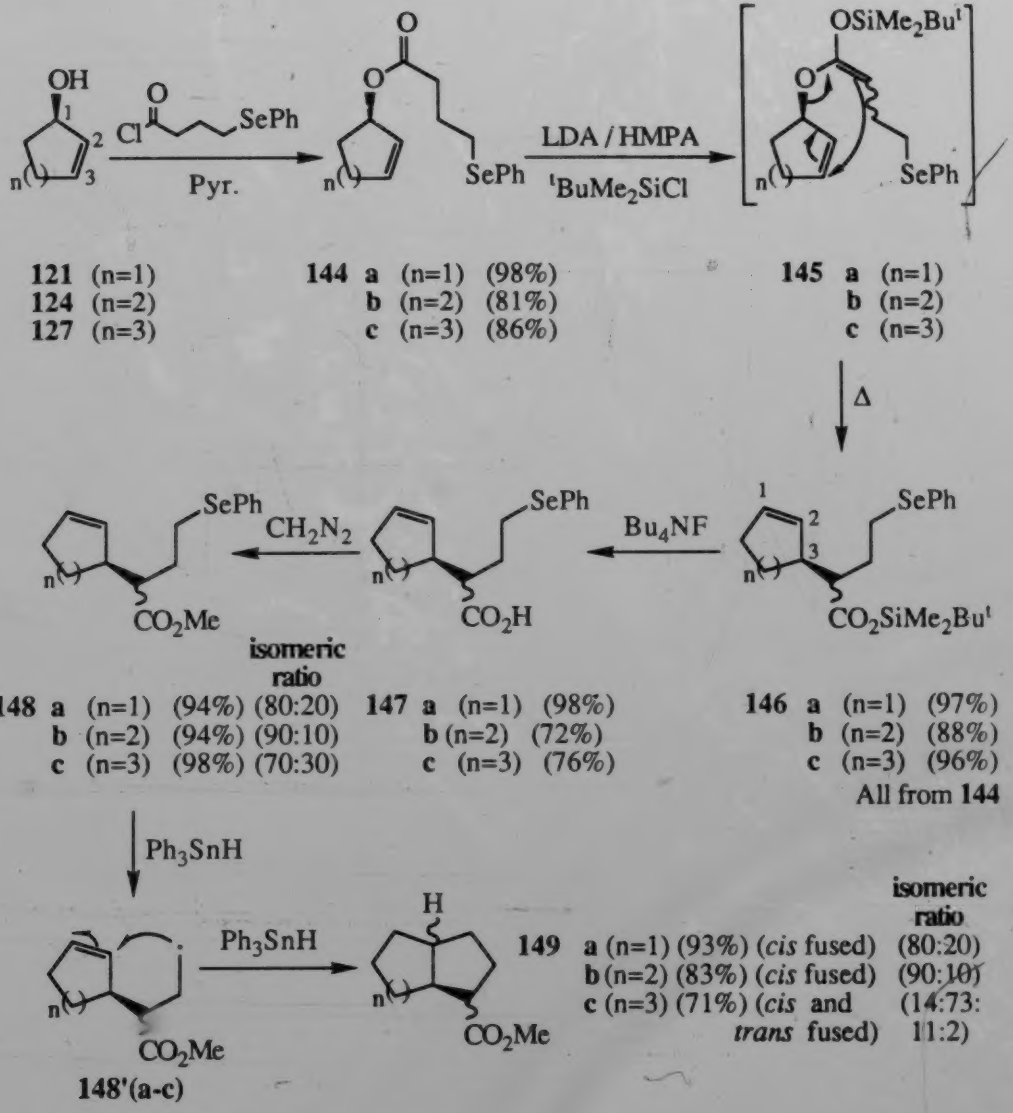
The acid chlorides required for our experiments were made from the corresponding γ and δ lactones (eq. 120).[176-178] Treatment of lactones **138** and **139** with PhSeNa produced high yields of the corresponding acids **140** and **141**. These acids were then converted in excellent yields to the required acid chlorides when treated with oxalyl chloride in benzene.



eq. 120

138 (n=1)
139 (n=2)
140 (n=3) (94%)
141 (n=4) (84%)
142 (n=3) (100%)
143 (n=4) (99%)

Scheme 16



121 (n=1)
124 (n=2)
127 (n=3)

144 **a** (n=1) (98%)
b (n=2) (81%)
c (n=3) (86%)

145 **a** (n=1)
b (n=2)
c (n=3)

146 **a** (n=1) (97%)
b (n=2) (88%)
c (n=3) (96%)
All from **144**

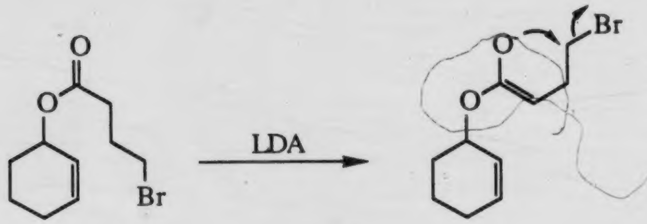
147 **a** (n=1) (98%)
b (n=2) (72%)
c (n=3) (76%)

isomeric ratio
148 **a** (n=1) (94%) (80:20)
b (n=2) (94%) (90:10)
c (n=3) (98%) (70:30)

148'(a-c)

isomeric ratio
149 **a** (n=1) (93%) (*cis* fused) (80:20)
b (n=2) (83%) (*cis* fused) (90:10)
c (n=3) (71%) (*cis* and *trans* fused) (14:73:11:2)

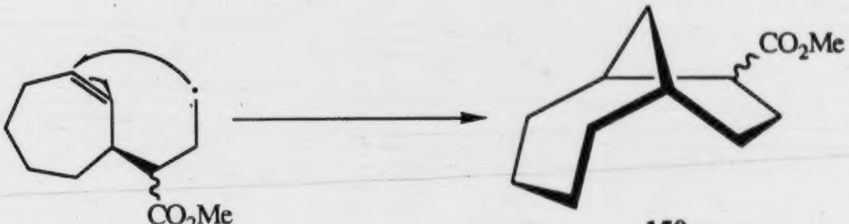
In the first step of our sequence (Scheme 16), the allylic alcohols were acylated using 4-(phenylseleno)butyroyl chloride **142** to give the corresponding esters. As can be seen, we used only the phenylseleno esters, because the second step is a deprotonation step and when a bromo ester was deprotonated it did not give us the desired result, the reason being that the enolate can displace the bromine in an intramolecular manner (eq 121) or by an intermolecular process. The phenylseleno group cannot be displaced and was used for this reason. The esters were then deprotonated with LDA to give mainly the enolate with the expected Z geometry.[129,131] Treatment of these enolates with TBSiCl/HMPA and then heating of the resulting silyl ketene acetals afforded the Claisen rearrangement products **146** in high yields. We found it convenient to modify the water-sensitive products **146** by desilylation using tetrabutylammonium fluoride followed by methylation with diazomethane to give methyl esters **148**. As indicated in Scheme 16, the isomeric ratio of methyl esters **148** obtained by the use of the Ireland rearrangement is usually higher than that obtained from the orthoester approach (Table 2).



eq.121

Subjecting these methyl esters to our radical cyclization conditions gave radicals **148'**. These radicals cyclized in an 5-*exo* fashion to the bicyclic products **149a-c** in high yields.

As stated earlier, our goal was to establish a method in which the stereochemical outcome would be controlled and predictable at all stages of the reaction scheme. In our sequence (Scheme 16) the main stereochemical features of the overall process are predictable: the selenium-substituted pendant (see **144**) is transferred suprafacially so that the stereochemistry at C(3) in **146** is determined by the stereochemistry at C(1) in the starting alcohol.[134,179] The nature of the ring fusion stereochemistry in **149a-c** depends on the value of n. In the cyclization producing **149a** a mixture (^{1}H NMR, 400 MHz) of the two isomers [epimeric[142b,137,139] at C(1), ca. 80:20] is obtained and we assigned the ring fusion as *cis* in both cases on the basis of the strong preference for this geometry.[180] In the case of **149b** again only two isomers [epimeric at (C1), ca. 90:10] were formed [^{1}H NMR, 400 MHz] as expected on the basis of precedent.[181] The *cis* nature of the ring fusion was clear from the ^{13}C NMR spectrum [100.62 MHz] of the material; none of the signals reported[182] for the *trans* ring-fused isomers were evident [signal:noise = 70:1 for most intense peak] and the signals actually present were assigned to the *cis*-fused esters by comparison with an authentic sample,[183a] the major isomer being that with 1α,3aβ,7aβ stereochemistry.* In contrast, **149c** was obtained as a mixture of four isomers (^{1}H NMR, 400 MHz, ca. 14:72:11:2) and we concluded that both *cis* and *trans* ring-fusion products are formed.[59,184] We were able to rule out structure **150**, which would



150

eq. 122

have involved 6-*endo* ring closure (eq. 122). An authentic sample of **150** was made as in (eq. 123) and used for comparison. The synthesis of **150** began with the known keto ester **151**.[183b] Reduction of **151** with triphenyltin hydride afforded keto ester **151'** which was converted to the thioacetal **152**[185] with boron trifluoride and ethanedithiol. Reduction of **152** using Raney Nickel gave **150** which had high field ^{1}H and ^{13}C NMR spectra totally different from that of the material obtained from the radical cyclization.

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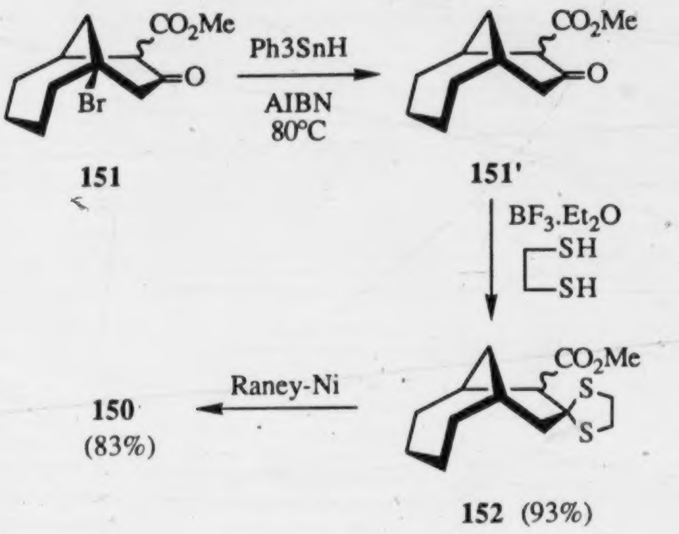
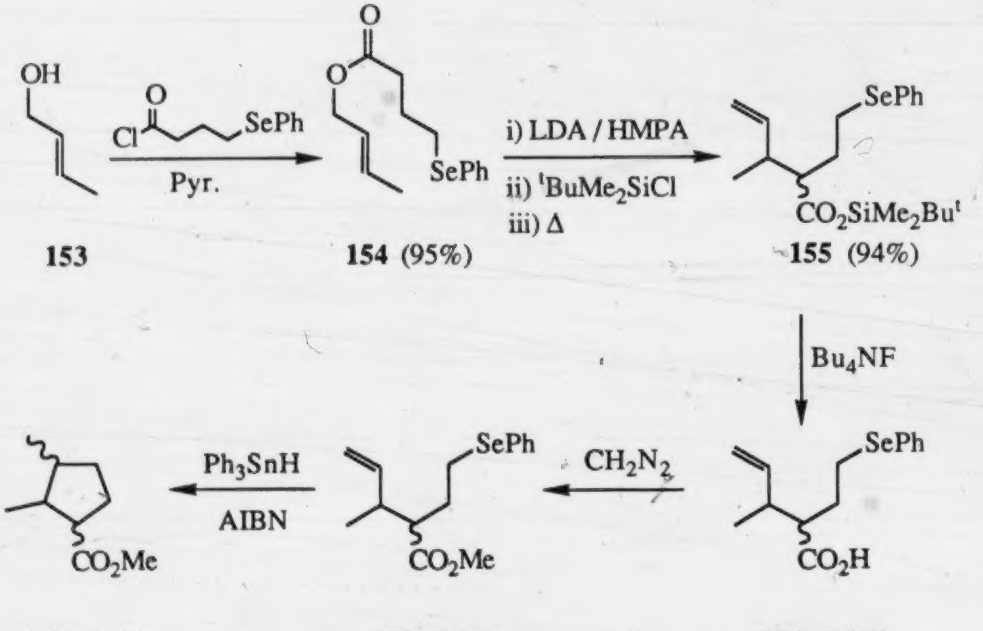
*The senior group (sequence rule) at (C1) defines the α-face.



eq. 123

Formation of **149a-c** can be described[184,186] as 5-exo-trigonal-[endo-5], 5-exo-trigonal-[endo-6], and 5-exo-trigonal-[endo-7]

Scheme 17



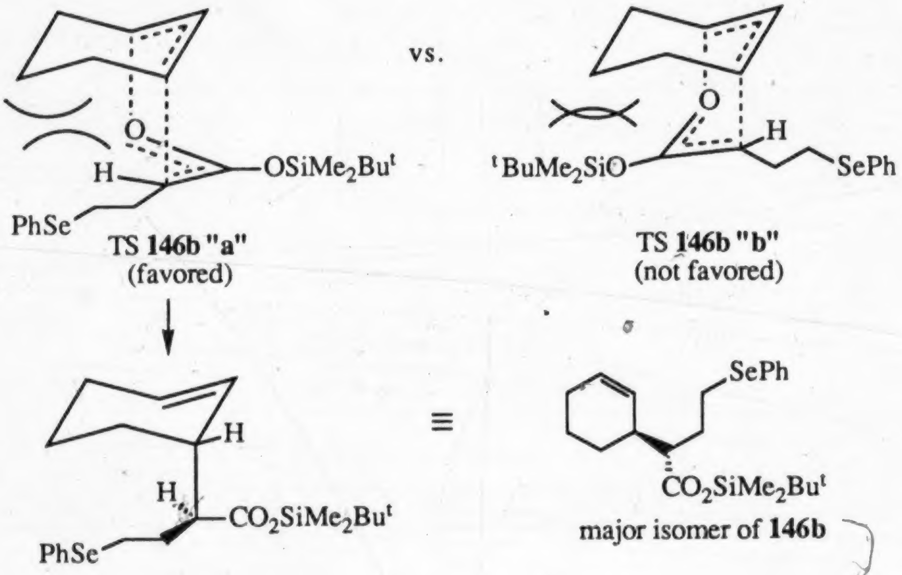
processes respectively, where the size of the ring originally associated with the endocyclic double bond is specified in brackets. There is evidently a kinetic barrier to the formation of *trans* ring-fused products, as follows:

Reaction type	*trans* Ring-fusion
5-exo-[endo-5]	Disfavored
5-exo-[endo-6]	Disfavored[187]
5-exo-[endo-7]	Allowed

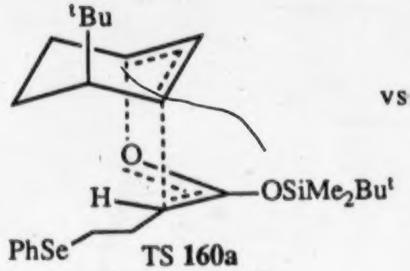
Similar regulations apply to ionic reactions such as halolactonization[188] and ring closure mediated by selenium reagents.[184]

We also demonstrated our methodology in two other cases. In the first one we used an acyclic allylic alcohol (Scheme 17). Crotyl alcohol **153** (containing ≤ 7% *cis* isomer) was converted to the corresponding ester **154** as described above, and then subjected to the conditions that induced Claisen rearrangement to the silyl ester **155**. Desilylation followed by methylation gave ester **157** which, upon treatment with triphenyltin hydride in the presence of an initiator, gave the methyl ester **158** as a mixture of four isomers (^{1}H NMR, 400 MHz). However, we did not establish whether the relative proportions are in accord with theory.[2,174]

In the second case (Scheme 18) we converted the rigid ester **160** to the rearranged silyl ester **162** as described above, except that thermolysis of the silylketene acetal **161** was carried out in toluene. Desilylation of **162** gave the acid **163** as a mixture of two epimers. These epimers were separated by flash chromatography. We assigned structure **165** to the major isomer (90% of total) on the basis of analogy with the major isomer from **146b** (see transition states below). However, when a similar transition state is

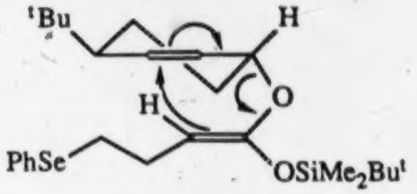


written for the rearrangement of **160**, i.e. with the oxygen atom in an axial orientation, this then will lead to transition state **160a** which is not likely to take place due to the great steric hindrance imposed by the *tert*-butyl group. However, if the oxygen atom is placed in a quasi equatorial position, as in transition state **160b** below,



TS **160a**
(very strained)

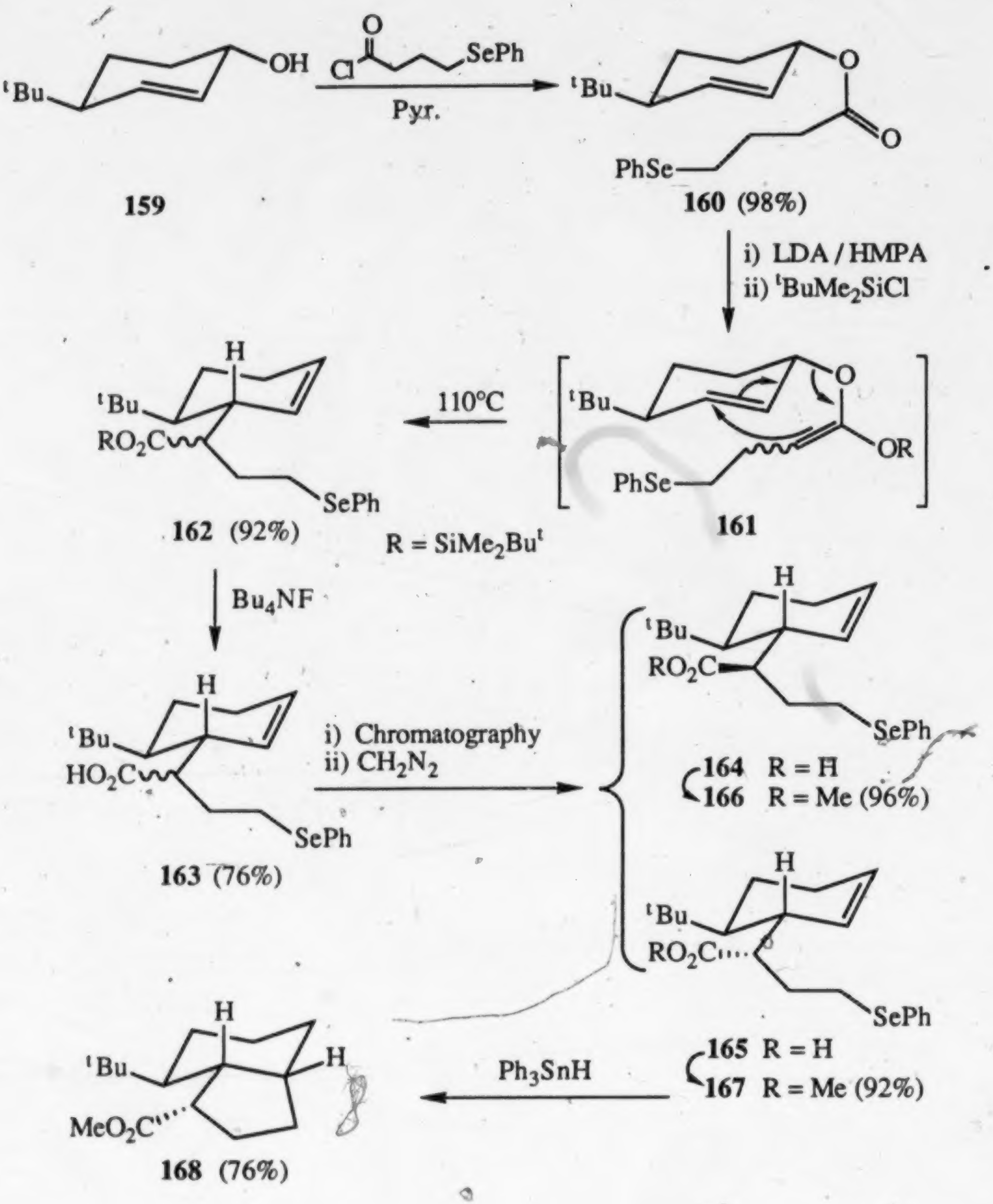
vs.



TS **160b**
(more favored)

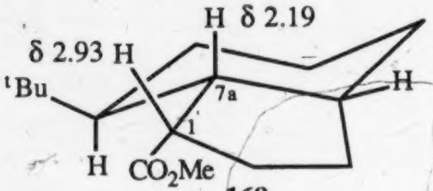
then the rearrangement from this particular orientation is less disfavored and should give rearranged material similar to that obtained from **146b**, as described above. Also the assignment was in agreement with decoupling and NOE experiments carried out on the final cyclized product **168** (see below). Methylation of both acids with diazomethane gave **166** and **167**, respectively. In all our previous examples, the ring was not substituted and so the molecule undergoing the cyclization cauld assume a variety of conformations. Models show that cyclization can easily take place when the pendant carrying the free radical is located in an axial orientation. In the present example, i.e. the cyclization of **167**, the pendant carrying the free radical is equatorial. Therefore, we studied this case to find out if a molecule having a pendant in an equatorial position could cyclize and we were pleased to find out that treatment of **167** with triphenyltin hydride gave one product. We assigned its structure as **168** on the basis of NOE and

Scheme 18

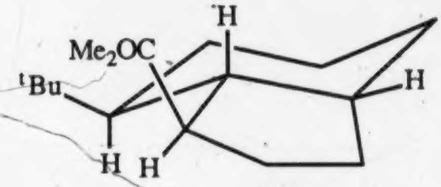

ᵗBu
OH
159
Cl
O
SePh
Pyr.
O
O
PhSe
160 (98%)
i) LDA / HMPA
ii) ᵗBuMe₂SiCl
O
OR
PhSe
161
110°C
H
ᵗBu
RO₂C
SePh
162 (92%)
R = SiMe₂Buᵗ
Bu₄NF
HO₂C
SePh
163 (76%)
i) Chromatography
ii) CH₂N₂
RO₂C
SePh
164 R = H
166 R = Me (96%)
165 R = H
167 R = Me (92%)
Ph₃SnH
MeO₂C
H
168 (76%)

decoupling experiments as described below. Therefore, we have demonstrated that even when a pendant is located at an equatorial position, it can indeed lead to a good yield of the cyclized product.

In the first decoupling experiment, we irradiated the signal at δ 2.19 and the pattern of the signal at δ 2.93 was simplified. In the second decoupling experiment, we irradiated at δ 2.93 and the signal at δ 2.19 changed from ddd to a broad triplet with J = 6.7 Hz (diagram 1).



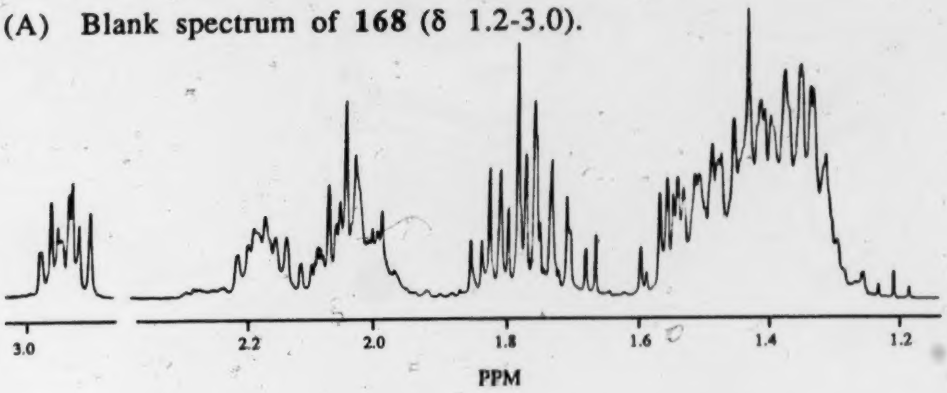
168



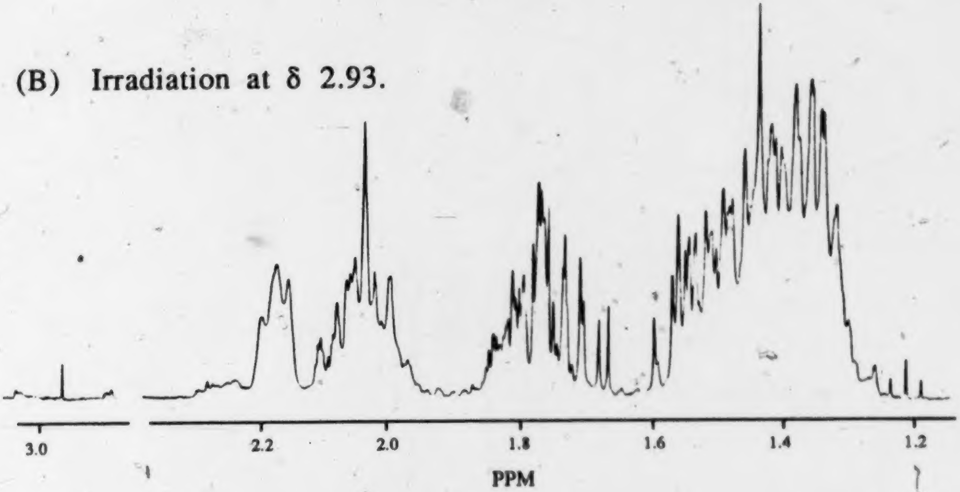
169

On the other hand, in the first NOE experiment we irradiated the signal at δ 2.19 and the signal at δ 2.93 was enhanced by 12.4%, also the signal at δ 1.76 was enhanced by 6.7%. In the second NOE experiment, we irradiated the signal at δ 2.93 and the signal at δ 2.19 was enhanced by 11.4%, also the signal at δ 1.76 was enhanced by 8.1%. This proved that the methyl carboxylate group is "α" as shown in structure **168**. Had it been "β" as in structure **169**, there would not be such an enhancement in the NOE experiments as the protons on C(1) and (C7a) will not be close to each other.

(A) Blank spectrum of **168** (δ 1.2-3.0).



(B) Irradiation at δ 2.93.



(C) Irradiation at δ 2.19.

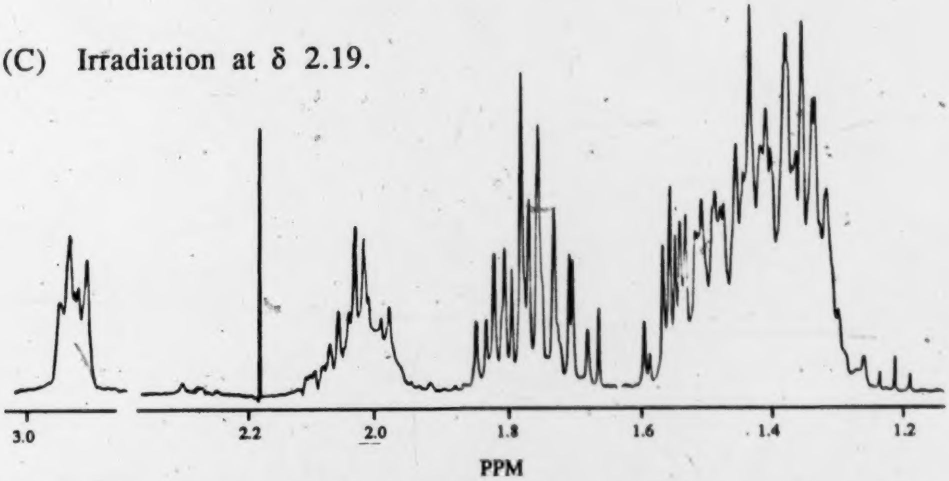
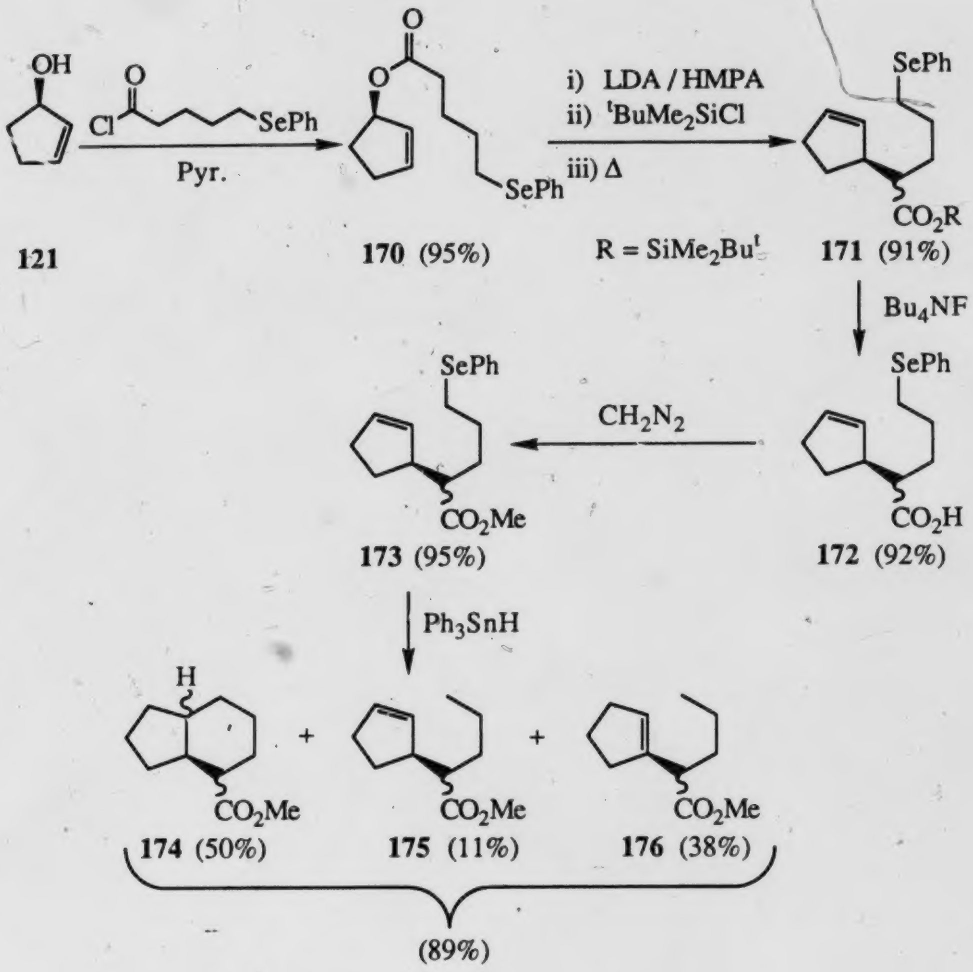
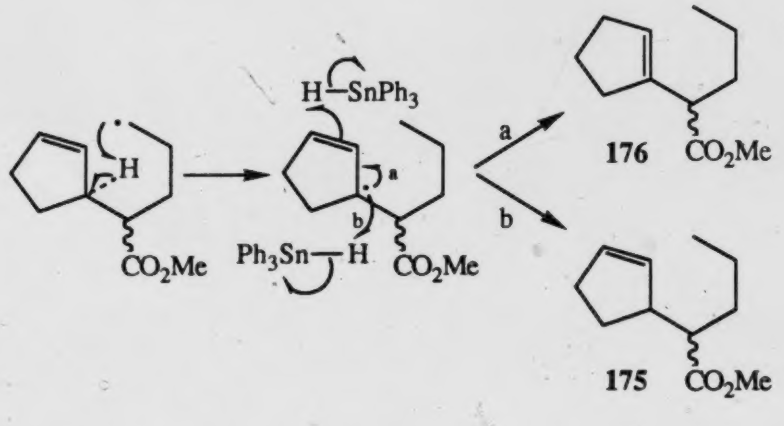


Diagram (1) Decoupling experiments on **168** (Spectra were recorded on Bruker WH-300 spectrometer).

Having been successful in making 5-membered carbocycles by the use of the Claisen rearrangement, we examined the possibility of effecting 6-exo ring closure (Scheme 19) using the same approach. Preparation of methyl ester **173** was carried out as outlined above and in excellent yield. However, when subjecting ester **173** to the radical cyclization conditions, we found the cyclization process was not efficient. Cyclization by a 6-exo pathway is known to be inherently slow[175] and so the result was not surprising. Also, our observation may reflect interference from intramolecular hydrogen transfer as in eq.124. We have not examined cases in which that pathway is blocked by substitution.

Scheme 19

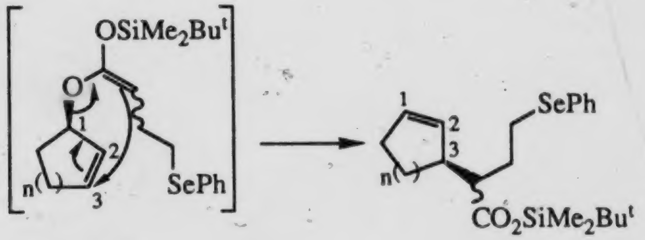




eq. 124

ii) PREPARATION OF NITROGEN HETEROCYLES:

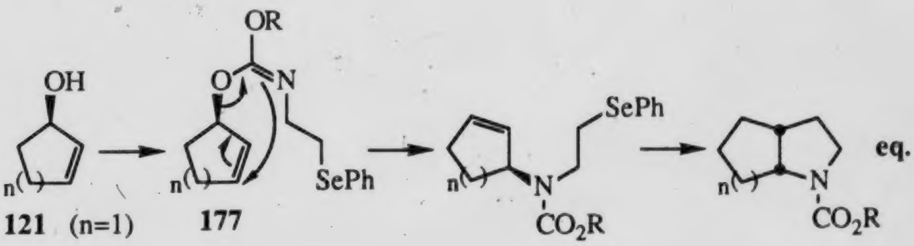
Our success in the chirality transfer from (C1) of allylic alcohols to (C3) by a suprafacial process (eq. 125) led us to envision



145 **146**

eq. 125

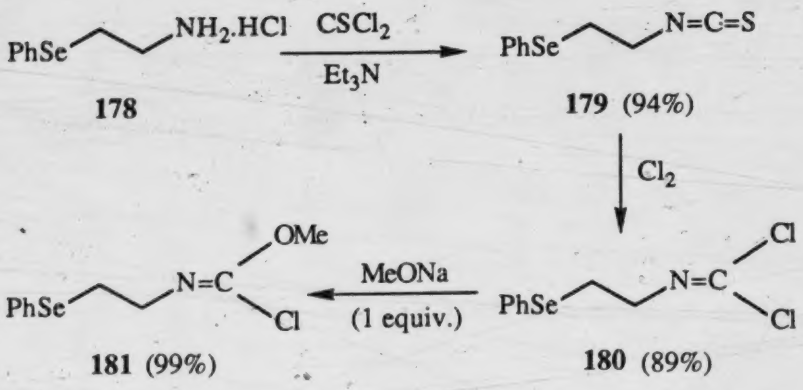
the possibility of converting allylic alcohols to 5-membered nitrogen heterocycles in a similar manner (eq. 126).



121 (n=1) **177**

eq. 126

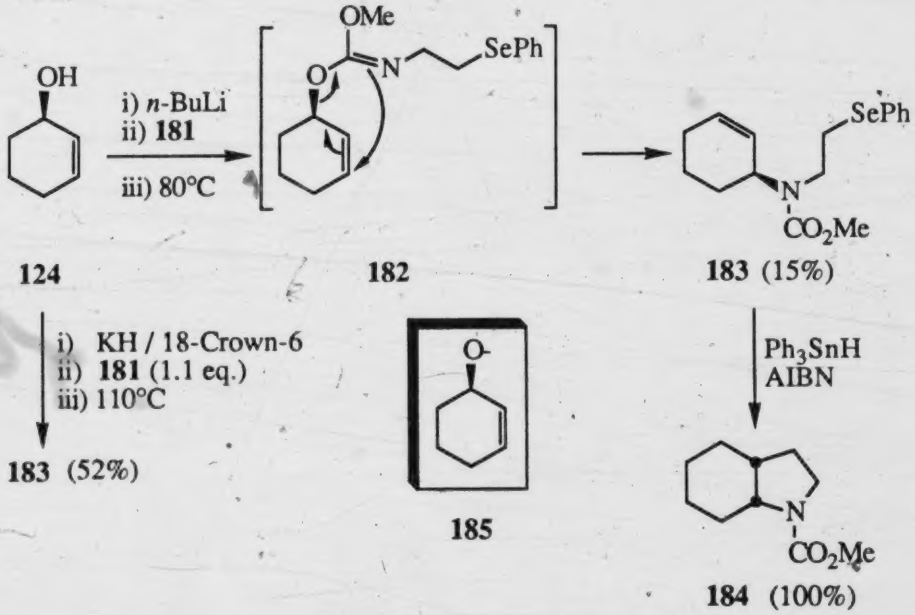
To convert **121** to **177** we had to use imidoyl chloride **181** which was made as outlined in eq. 127. The amine hydrochloride **178**[189] was converted to isothiocyanate **179** by thiophosgene and triethylamine.[190] Chlorination of **179** using chlorine gas gave carboimidoyl dichloride **180** which, upon treatment with one equivalent of sodium methoxide, gave imidoyl chloride **181**.



eq. 127

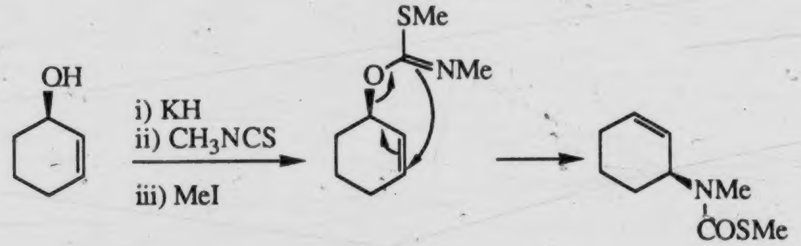
We attempted the conversion of allylic alcohol **124** to the corresponding carbamate **183** (Scheme 20) using the aza Claisen rearrangement. In our first attempt, we used *n*-butyllithium as our base to deprotonate the allylic alcohol **124**. The resulting allyl oxide was then treated with the imidoyl chloride **181** to afford

Scheme 20



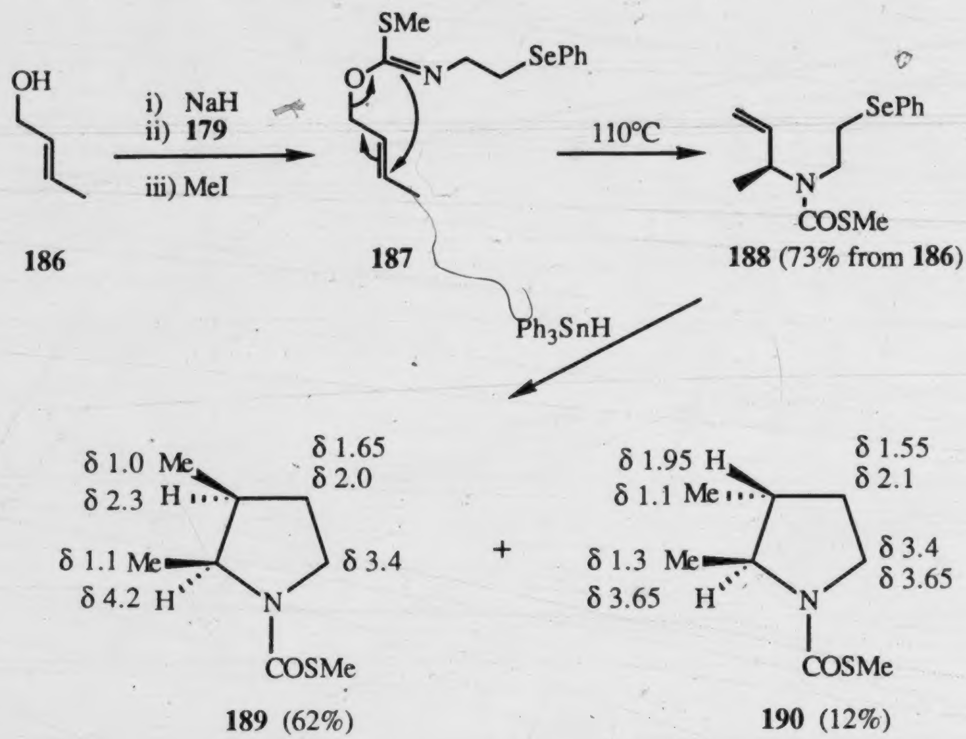
intermediate **182**, which upon thermolysis gave the corresponding carbamate **183**; however, it was produced in a low yield. We attributed that to inefficient coupling of **124** with the imidoyl chloride **181**. Therefore we changed our coupling conditions (Scheme 20) to the use of KH/18-crown-6 to make the oxygen of the allyl oxide **185** more nucleophilic. Also we raised the rearrangement temperature in order to increase the rate of rearrangement. These changes led to a moderate yield (52%) of **183**. At this juncture we thought that a more efficient method was needed to accomplish our first task, namely the rearrangement, as we were confident that the radical cyclization step would work. In fact we obtained a 100% yield of **184** when the carbamate **183** was subjected to our radical cyclization conditions. As expected, we obtained the *cis*-fused bicyclic system **184**.

We then decided to study the reported rearrangement[191] to thiocarbamates (eq. 128) and we attempted to carry out our rearrangement using this method (Scheme 21).



eq. 128

Scheme 21



Crotyl alcohol was converted to the corresponding thiocarbamate by deprotonation with NaH, addition of the isothiocyanate **179**, quenching with MeI, and then heating at 110°C for 19 h. Thiocarbamate **188** was obtained in a good yield and was subjected to conditions that induced radical cyclization to give pyrrolidines **189** and **190** respectively. We were able to separate these two stereoisomers by flash chromatography and we assigned the major isomer to the *cis* material **189** and the minor isomer to the *trans* material **190** on the basis of decoupling and NOE experiments:

Isomer 189:

I- Decoupling:

1- Irradiation δ 2.3 made the signal at δ 1.0 collapse to a singlet and also simplified the signals at δ 1.65 and δ 2.0.

2- Irradiation at δ 2.0 simplified the signals at δ 1.65 and δ 2.3.

3- Irradiation at δ 1,1 converted the signal at δ 4.2 into a doublet, J = 7.6 Hz.

4- Irradiation at δ 1.0 simplified the signal at δ 2.3.

II- NOE:

1- Irradiation at δ 1.0 enhanced the signal at δ 2.3 by 10%.

2- Irradiation at δ 1.1 enhanced the signal at 4.2 by 19%.

Isomer 190:

I- Decoupling:

1- Irradiation at δ 1.1 simplified the signal at δ 1.95.

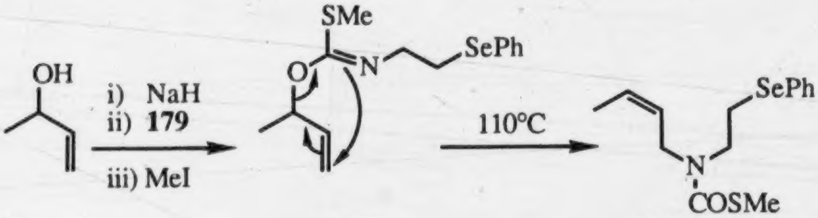
2- Irradiation at δ 1.3 simplified the signals at δ 3.4 and δ 3.65.

II- NOE:

1- Irradiation at δ 1.3 enhanced the signals at δ 3.65 by 11% and at δ 1.95 by 5%.

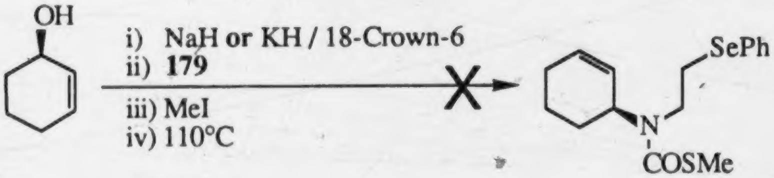
2- Irradiation at δ 1.1 enhanced the signals at δ 3.65 by 11% and at δ 1.95 by 5%.

However, when we attempted to further examine this method using secondary allylic alcohol **191** (eq. 129), the rearrangement was not as promising as expected. Also the rearrangement failed when using cyclohexenol as the starting allylic alcohol (eq. 130).



191 **192** **193** (20% from **191**)

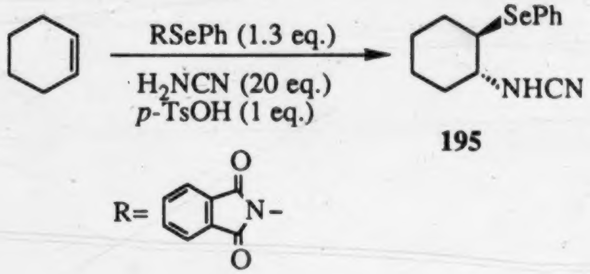
eq. 129



124 **194**

eq. 130

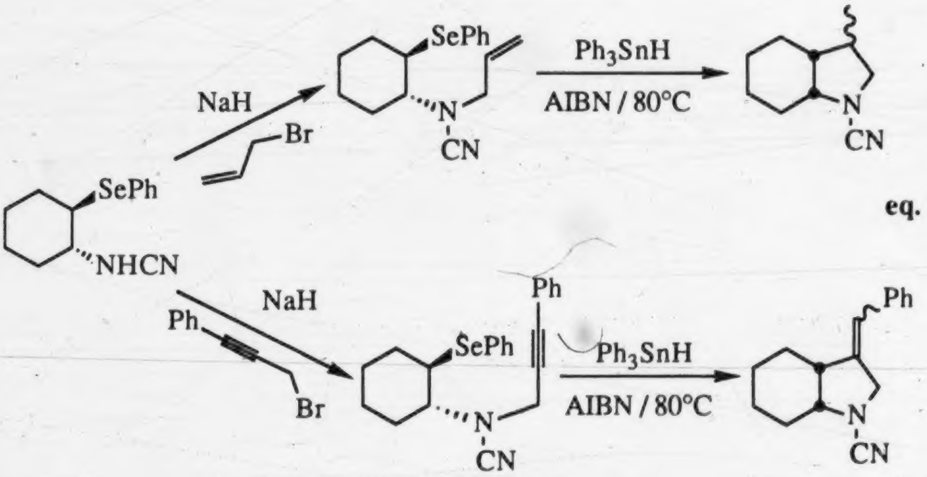
At this point we abandoned this approach and shifted our attention to a new method for making 5-membered nitrogen heterocycles. This new method uses olefins as the starting materials (eq. 131).



195

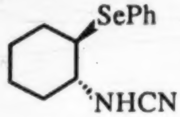
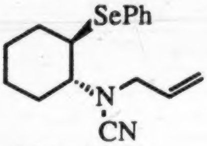
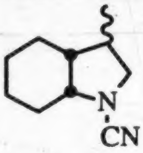
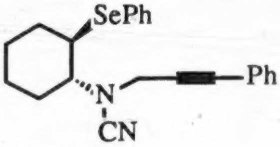
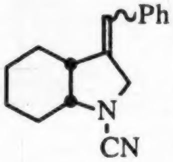
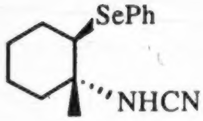
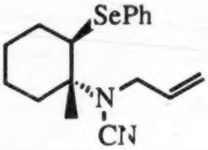
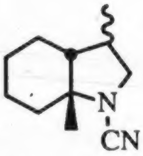
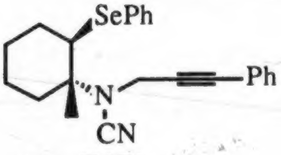
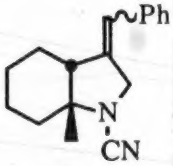
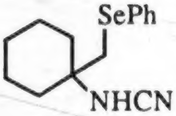
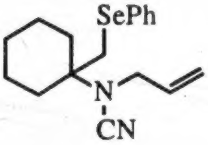
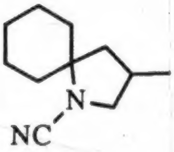
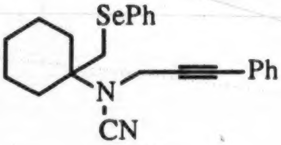
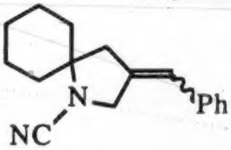
eq. 131

In the first step, olefins were converted to β-aza selenides.[192,193] This was possible through the reaction of *N*-(phenylseleno)-phthalimide with olefins in the presence of cyanamide according to the stoichiometry of eq. 131. The resulting 2-(phenylseleno)alkyl cyanamides were suited for attachment of an unsaturated alkyl chain on the amino nitrogen. This was achieved by deprotonation with NaH and alkylation with an allylic or propargylic bromide (eq. 132) (Table 3).



eq. 132

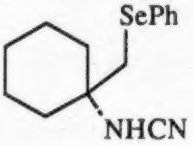
Table 3.[a] Synthesis of 5-membered nitrogen heterocycles

Starting material	Alkylation Product	Cyclization Product
 **195**[b] (80%)	 **196** (91%)	 **197**[c] (97%)
	 **198** (85%)	 **199**[c] (87%)
 **200**[d] (82%)	 **201** (93%)	 **202** (95%)
	 **203** (74%)	 **204**[c] (85%)
 **205**[e] (67%)	 **206** (79%)	 **207** (66%)
	 **208**[f] (62%)	 **209**[g]

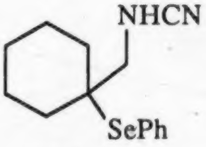
Footnotes to Table 3

[a] Yields refer to pure isolated compounds. [b] From cyclohexene. [c] Two isomers. [d] From 1-methylcyclohexene. [e] From methylenecyclohexane. Compound **205** was formed together with the isomer [[1-(phenylseleno)cyclohexyl]methyl]cyanamide **205'**. Yield refers to mixture of **205** and **205'**. [**205**:**205'**::92:8]. [f] Yield based on amount of **205** in starting mixture of **205** and **205'**. [g] We were unable to obtain this compound pure.

The initial addition of the benzeneseleno group and the nitrogen function across the double bond is sometimes highly regioselective with unsymmetrical olefins, but this was not the case with methylene cyclohexane. Our impression is that the ratio of **205:205'** is sensitive to the quality of *N*-(phenylseleno)phthalimide. With high quality material we achieved a ratio of 92:8; however other commercial batches of *N*-(phenylseleno)phthalimide gave a poor (66:34) ratio.



205



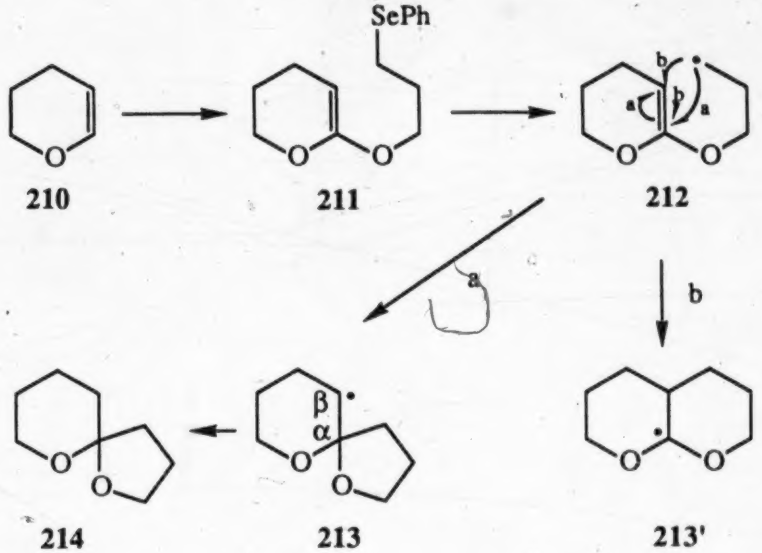
205'

In all of our examples, the alkylation step worked smoothly with yields of 62-93% (Table 3). Radical cyclization of the dialkylcyanamides went very smoothly, as we expected, but with one exception and that was compound **209**. Attempts to carry out the radical cyclization to form **209** were not successful. However, we did obtain some spectroscopic evidence (^{1}H NMR) for the production of the desired azaspirodecane **209**.

iii) STUDIES TOWARD THE SYNTHESIS OF SPIRO ETHERS:

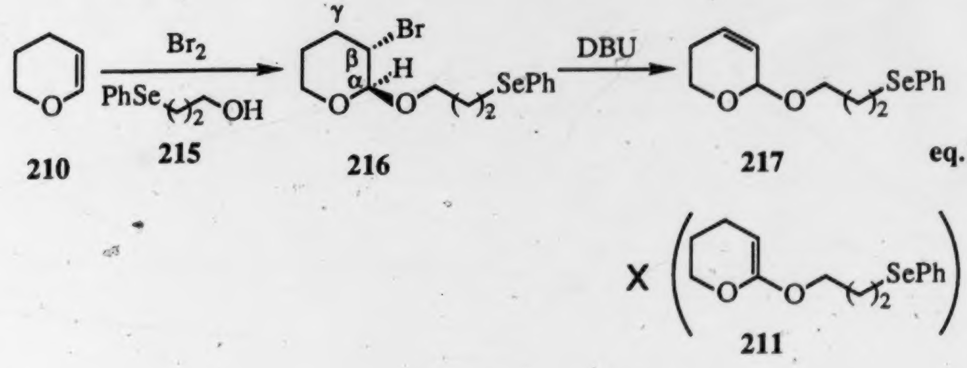
We also examined the possibility of making spiro ethers by radical cyclization as outlined in Scheme 22.

Scheme 22



Although the desired cyclization (**212** to **213**) is onto a tertiary center via a 5-*exo* closure (path a), the resulting radical is stabilized by the β-oxygen effect[194] and we wanted to determine experimentally if path **a** would be favoured over path **b**.

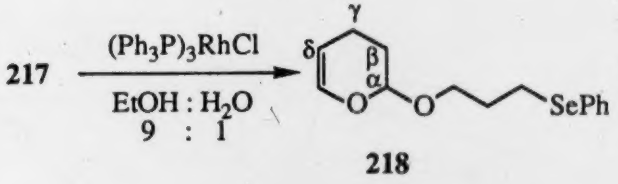
Our target then was to synthesize compound **211**. The first approach we tried was to make compound **216** (eq. 133). It was obtained from dihydropyran, bromine and alcohol **215**.[195]



eq.133

However, when we subjected **216** to the action of base in the hope of effecting a β elimination to **211**, we obtained instead compound **217**. The reason for this result is that the proton at the α position is *syn* to the bromine, and for fast elimination we need an *anti* orientation. We had hoped that due to the higher acidity of the proton at the α position, we might observe *syn* elimination, but this was not the case.

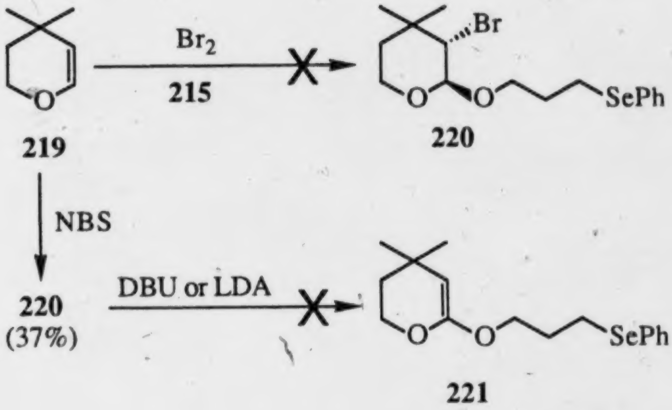
Having **217** in hand, we decided to move the double bond from the β position to the α location using Wilkinson's catalyst. After carrying out the experiment, we found that the double bond had indeed migrated but to the δ position instead of the α position (eq.134).



eq. 134

We then attempted to make the system **221** in which the γ position is blocked so as to force a *syn* elimination. This route is outlined in Scheme 23. In this attempt, we used 4,4-dimethyl dihydropyran **219**.[196] Treatment of **219** with bromine and alcohol **215** did not produce the desired product; however, when NBS was used, we did obtain compound **220**, but in low yield. Nevertheless, we attempted to carry out the *syn* elimination. However, neither the action of LDA or DBU gave **221**. We have not investigated this sequence further.

Scheme 23



III- EXPERIMENTAL

Unless otherwise stated, the following particulars apply. Experiments were carried out under argon purified by passage through a column (35 x 42 cm) of R311 catalyst (Chemical Dynamics Corp.) and then dried through a similar column of Drierite.

Glassware was dried in an oven for at least 2 h (115°C), cooled in a desiccator, assembled quickly and sealed with rubber septa (where applicable). Inlet and exit needles were passed through the septa on the apparatus and argon was purged through the system. The exit needle was removed after a few minutes and the apparatus was kept under a slight static pressure of argon (provided no gas was being generated during the reaction). Stirring was effected by using a dry, Teflon-coated magnetic stirring bar.

Materials were weighed quickly into dry flasks which were then sealed with rubber septa and purged with argon. Transfer of moisture- and/or air-sensitive reagents was accomplished using dry, well-greased syringes whenever possible, solids being dissolved in a suitable solvent prior to transfer. Solvents were distilled for chromatography. Where required, solvents and reagents were dried with suitable drying agents and distilled under argon. Dry ether, tetrahydrofuran and dioxane were distilled from sodium-benzophenone ketyl; benzene and toluene were distilled from sodium; dichloromethane, chloroform, carbon tetrachloride, hexane, pyridine, triethylamine, diisopropylamine and acetonitrile were distilled from calcium hydride. Methanol was distilled from magnesium methoxide; U.S.P. absolute ethanol was used without further drying. Commercial solutions (Aldrich) of *n*-butyllithium in hexanes were titrated by use of the diphenylacetic acid method. Azobisisobutyronitrile (AIBN) was stored at 0°C and used without further purification.

Products were isolated from solution by concentration under water aspirator vacuum at *ca.* 30°C using a rotary evaporator. Melting points were measured using a Kofler block.

Commercial silica (Merck 60F-254) thin layer chromatography (TLC) plates were used. Silica gel for flash chromatography was Merck type 60 (230-400 mesh). TLC plates were examined under uv radiation (254 nm), treated with iodine vapor or charred on a hot plate after being sprayed with a solution of either i) phosphomolybdic acid (prepared from phosphomolybdic acid (3g, $MoO_3. 2H_3PO_4.48H_2O$) and ceric sulphate [0.5 g, $H_4Ce(SO_4)_4$] in 100 mL of 3% aqueous H_2SO_4 ii) a solution of anisaldehyde (15 drops) in a 94:6 solution of absolute ethanol:concentrated sulfuric acid or iii) Dragendorff's reagent [made by mixing solution **A** {1.7 g basic $Bi(NO_3)_3$ in water-acetic acid solution (80:20) (100 mL)} (20 mL) and solution **B** {40 g potassium iodide in water (100 mL)} (5 mL)].

Elemental combustion analyses were performed in the microanalytical laboratories of the University of Alberta. Infrared spectra were recorded on a Perkin-Elmer 297 spectrophotometer or a Nicolet 7000 FT-IR instrument. Proton NMR were recorded on Bruker WP-80 (at 80 MHz), Bruker WH-200 (at 200 MHz), Bruker WH-300 (at 300 MHz) and Bruker WH-400 (at 400 MHz) instruments. ^{13}C NMR spectra were recorded on the latter three instruments at 50.3, 75.5 and 100.6 MHz respectively. All spectra were recorded in deuterated chloroform or other deuterated solvents with TMS as an internal standard. The following abbreviations are used in the text: s, singlet; d, doublet; t triplet; q, quartet; q', quintet; se, sextet; m, multiplet; J, coupling constant; δ, chemical shift.

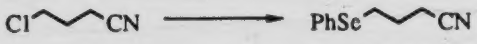
Mass spectra were recorded on an A.E.I. MS 50 mass spectrometer at an ionizing potential of 70 EV. All compounds with asymmetric centers are racemic unless otherwise stated.

Boiling points reported for liquids that were distilled in a Kugelrohr apparatus refer to the oven temperature.

General procedure for radical cyclization

Oven-dried apparatus and anhydrous solvents were used. A 100-ml round-bottomed flask containing a Teflon-coated magnetic stirring bar and equipped with a reflux condenser fitted with a rubber septum was purged with argon and immersed in an oil bath preheated to 80°C. A benzene solution of the substrate (0.01-0.02 M) was injected into the flask and then benzene solutions of triphenyltin hydride (1.1-1.25 equivalent, 0.7-0.1 M) and of azobisisobutyronitrile (AIBN) (Eastman, 0.05 equivalent, 0.003 M) were added simultaneously by double syringe pump over a period of 12-15 h. Refluxing was continued for an arbitrary period of 3 h after the end of the addition and the solvent was then evaporated. The residue was processed as described for the individual examples.

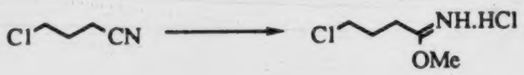
4-(Phenylseleno)butyronitrile 117c.[197]



The following procedure is based on a general method.[111] Sodium borohydride (2.00 g, 52 mmol) was added in batches to a magnetically stirred solution of diphenyl diselenide (1.745 g, 5.59 mmol) in ethanol (25 mL) kept at 0°C and under nitrogen. 4-Chlorobutyronitrile (1.158 g, 11.18 mmol) in ethanol (2 mL) was then injected dropwise at 0°C and the mixture was stirred for 30 min after the end of the addition. The solvent was evaporated and the residue was extracted with ether (3 x 25 mL). The ethereal layer was dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (5 x 15 cm) using 9:1 hexane-ethyl acetate afforded **117c** (2.305 g, 92%) as a homogenous (TLC, silica, 9:1 hexane-ethyl acetate), yellow oil:[197] IR ($CHCl_3$, cast) 2247 cm^{-1}; ^1H

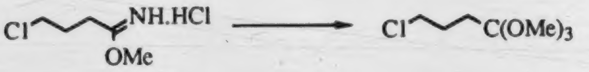
NMR ($CDCl_3$, 80 MHz) δ 2.05 (q', J = 7 Hz, 2 H), 2.53 (t, J = 7 Hz, 2 H), 3.05 (t, J = 7 Hz, 2 H), 7.27-7.75 (m, 5 H).

Methyl 4-Chlorobutanimidate hydrochloride 118a.



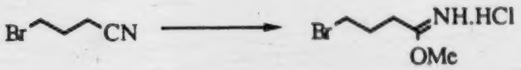
The following procedure is based on a general method.[111] Dry HCl was bubbled into a solution of 4-chlorobutyronitrile (3.143 g, 30.37 mmol) and dry methanol (1.33 mL, 33.00 mmol) in ether (30 mL) at -20°C. When the solution was saturated with HCl, the mixture was kept at -20°C for 4 days. At this stage white crystals had formed. These were filtered off under argon to yield the imidate hydrochloride **118a** (4.893 g, 93%): IR ($CHCl_3$, cast) 2944 (broad and strong), 2420 (broad and strong), 1492 (broad and medium) cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 2.00-2.65 (m, 2 H), 2.75-3.10 (m, 2 H), 3.61 (t, J = 6 Hz, 2 H), 4.32 (s, 3 H), 11.68 (broad s, 1 H), 12.62 (broad s, 1 H).

1-Chloro-4,4,4-trimethoxybutane 119a.[198]



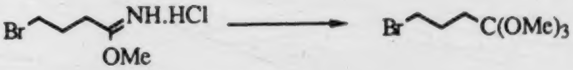
The following procedure is based on a general method.[111] Methanol (11.0 mL, 272 mmol) was added to a suspension of imidate hydrochloride **118a** (9.90 g, 57.56 mmol) in dry hexane (50 mL) and the reaction mixture was stirred at room temperature for 18 h. Triethylamine (0.5 mL) was added, the mixture was filtered, and the solvent was evaporated. Kugelrohr distillation of the residue yielded orthoester **119a** (9.030 g, 85 %) as a clear, pure (^{1}H NMR) liquid: bp 30-32°C (0.05 mm); IR ($CHCl_3$, cast) 2940, 2832, 1465, 1301, 1277, 1150, 963, 923 cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 1.80-2.00 (m, 4 H), 3.30 (s, 9 H), 3.50-3.75 (m, 2 H).

Methyl 4-Bromobutanimidate hydrochloride 118b.



The procedure employed for imidate **118a** was followed using 4-bromobutyronitrile (1.50 g, 10.14 mmol) and methanol (0.45 mL, 11.12 mmol) in ether (10 mL) at -20°C. The imidate **118b** (2.978 g, 92%) was obtained as white crystals: IR ($CHCl_3$, cast) 2820 (broad and strong), 1703, 1460, 1400, 1113, 876 cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 2.34 (q, J = 7 Hz, 2 H), 3.02 (t, J = 7 Hz, 2 H), 3.51 (t, J = 7 Hz, 2 H), 4.38 (s, 3 H), 11.63 (broad s, 1 H), 12.58 (broad s, 1 H).

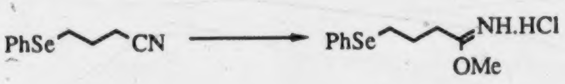
1-Bromo-4,4,4-trimethoxybutane 119b.[199]



The procedure employed for orthoester **119a** was followed using methanol (12 mL, 296 mmol) and imidate hydrochloride **118b**

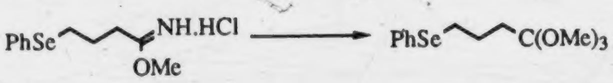
(10.50 g, 48.50 mmol) in hexane (75 mL). Kugelrohr distillation afforded orthoester **119b** (8.50 g, 86 %) as a clear, pure (^{1}H NMR) liquid: bp 47-48°C (0.05 mm); IR ($CHCl_3$, cast) 2947, 2840, 1437, 1368, 1298, 1152, 957, 927 cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 1.90-2.10 (m, 4 H), 3.35 (s, 9 H), 3.43-3.65 (m, 2 H).

Methyl 4-(Phenylseleno)butanimidate hydrochloride 118c.



The procedure employed for imidate **118a** was followed using 4-(phenylseleno)butyronitrile (1.80 g, 8.04 mmol) and methanol (0.35 mL, 8.65 mmol) in ether (10 mL) at -20°C. The imidate **118c** (2.135 g, 90%) was obtained as white crystals: IR ($CHCl_3$, cast) 2940 (broad), 2840 (broad), 1650, 1575, 1460, 1397, 1100, 667 cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 1.90-2.35 (m, 2 H), 2.75-3.12 (m, 4 H), 4.30 (s, 3 H), 7.20-7.65 (m, 5 H), 12.08 (broad s, 2 H).

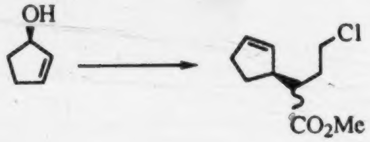
[(4,4,4-Trimethoxybutyl)seleno]benzene 119c.



The procedure employed for orthoester **119a** was followed using methanol (5 mL, 123 mmol) and imidate hydrochloride **118c** (5.50 g, 18.10 mmol) in hexane (70 mL). Kugelrohr distillation gave orthoester **119c** (5.301 g, 96 %) as a clear, pure (^{1}H NMR) liquid: bp

105°C (0.005 mm); IR ($CHCl_3$, cast) 3072, 3052, 2954, 2835, 1735, 1684, 1476, 1436, 1364, 1240, 1170, 1155, 1022, 736, 691 cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 1.75-2.10 (m, 4 H), 2.8-3.13 (m, 2 H), 3.33 (s, 9 H), 7.25-7.72 (m, 5 H); exact mass, *m/z* calcd for $C_{13}H_{20}O_3Se$ 304.0577, found 304.0586.

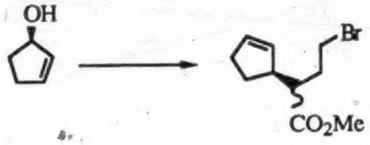
Methyl 2-(2-Cyclopenten-1-yl)-4-chlorobutanoate 122a.



The following procedure is based on a general method.[111] A mixture of orthoester **119a** (0.983 g, 5.40 mmol), 2-cyclopenten-1-ol (0.307 g, 3.64 mmol) and trimethylacetic acid (0.030 g, 0.29 mmol) in mesitylene (10 mL) was refluxed under argon at 160°C for 24 h. Evaporation of the solvent and flash chromatography of the residue over silica gel (5 x 15 cm) using first pure hexane to remove all the mesitylene and then increasing the polarity of the eluent to 10:1 hexane-ethyl acetate followed by Kugelrohr distillation gave esters **122a** (0.737 g, 88%) as an apparently homogenous (TLC, silica, 9:1 hexane-ethyl acetate), colorless oil: bp 140°C (water pump); FT-IR ($CHCl_3$, cast) 1734 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.54-1.66 (m, 1 H), 1.75-2.66 (m, 6 H), 2.98-3.07 (m, 1 H), 3.42-3.50 (m, 1 H), 3.55-3.64 (m, 1 H), 3.67 (s), 3.73 (s), [both signals (ratio 40:60) together have an area which corresponds to 3

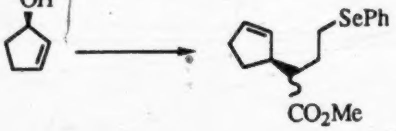
H], 5.55 (dq, J = 2.0, 5.5 Hz), 5.68 (dq, 2.0, 5.5 Hz), [both signals together have an area which corresponds to 1 H], 5.80-5.90 (m, 1 H); exact mass, *m/z* calcd for $C_{10}H_{15}ClO_2$ 202.0761, found 202.0765.

Methyl 2-(2-Cyclopenten-1-yl)-4-bromobutanoate 122b.



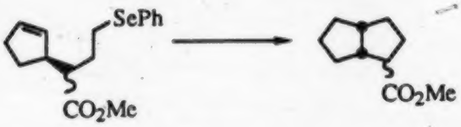
The procedure employed for esters **122a** was followed using 2-cyclopenten-1-ol (0.139 g, 1.66 mmol), orthoester **119b** (0.621 g, 2.74 mmol) and trimethylacetic acid (0.02 g, 0.2 mmol) in mesitylene (7 mL). After a reflux period of 24 h, the solvent was evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm) followed by Kugelrohr distillation afforded esters **122b** (0.103 g, 25%) as an apparently homogenous (TLC, silica, 9:1 hexane-ethyl acetate), colorless oil: bp 88°C (water pump); FT-IR ($CHCl_3$, cast) 1724 cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 1.63-2.70 (m 8 H), 3.48 (t, J = 6 Hz, 2 H), 3.69 (s, 3 H), 5.55-6.10 (m, 2 H).

Methyl 2-(2-Cyclopenten-1-yl)-4-(phenylseleno) butanoate 122c.



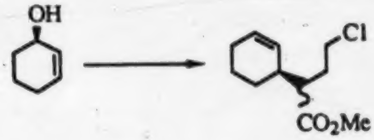
The procedure employed for esters **122a** was followed using 2-cyclopentene-1-ol (0.225 g, 2.67 mmol), orthoester **119c** (1.202 g, 3.95 mmol) and trimethylacetic acid (0.02 g, 0.2 mmol) in mesitylene (7 mL). After a reflux period of 24 h the solvent was evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm) followed by Kugelrohr distillation afforded esters **122c** (0.353 g, 41%) as an apparently homogenous (TLC, silica, 9:1 hexane-ethyl acetate), slightly yellowish oil: bp 107°C (0.03 mm); FT-IR ($CHCl_3$, cast) 1730 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.52 (dqd, J = 9, 13, 6.5 Hz, 1 H), 1.77-1.90 (m, 1 H), 1.91-2.02 (m, 1 H), 2.04-2.15 (m, 1 H), 2.20-2.37 (m, 2 H), 2.42-2.56 (m, 1 H), 2.77 (ddd, J = 11.5, 9.5, 7.0 Hz, 1 H), 2.90-3.03 (m, 2 H), 3.66 (s), 3.68 (s), [both signals (ratio 50:50) together have an area which corresponds to 3 H], 5.50 (dq J = 2, 6 Hz), 5.61 (dq, J = 2, 6 Hz), [both signals together have an area which corresponds to 1 H], 5.74-5.80 (m, 1 H), 7.18-7.28 (m, 3 H), 7.44-7.52 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 25.33, 25.40, 27.11, 27.29, 30.20, 30.43, 31.70, 31.90, 47.62, 47.88, 50.30, 51.22, 51.26. 126.68, 128.89, 129.93, 129.97, 131.40, 131.91, 132.02, 132.29, 132.38, 132.43, 174.95; exact mass, *m/z* calcd for $C_{16}H_{20}O_2Se$ 324.0628, found 324.0631.

Methyl (3aα,6aα)-Octahydro-1-pentalenecarboxylate 123 from 122c.



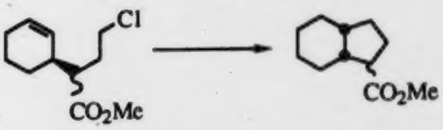
The general procedure for radical cyclization was followed using esters **122c** (0.301 g, 0.93 mmol) in benzene (50 mL), triphenyltin hydride (0.366 g, 1.10 mmol) in benzene (10 mL) and AIBN (10 mg, 0.07 mmol) in benzene (10 mL). After workup, flash chromatography of the residue over silica gel (2.5 x 15 cm) using 99:1 hexane-ethyl acetate followed by Kugelrohr distillation afforded esters **123** (0.110 g, 70%) as an apparently homogenous (TLC, silica, 9:1 hexane -ethyl acetate), colorless oil: bp 70°C (4.5 mm); FT-IR ($CHCl_3$, cast) 1729 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.05-1.40 (m, 3 H), 1.41-2.03 (m, 7 H), 2.28-2.38 (m, 1 H), 2.60-2.80 (m, 2 H), 3.67 (s), 3.68 (s), [both signals (ratio 50:50) together have an area which corresponds to 3 H]; ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 25.40, 26.49, 27.46, 29.91, 31.44, 31.87, 32.99, 33.44, 33.50, 34.97, 42.87, 43.38, 45.64, 47.86, 48.63, 51.18, 51.48, 51.77; exact mass, *m/z* calcd for $C_{10}H_{16}O_2$ 168.1150, found 168.1148. Anal Calcld for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.31; H, 9.53.

Methyl 2-(2-Cyclohexene-1-yl)-4-chlorobutanoate **125a.**



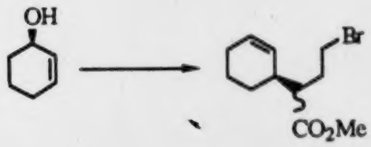
The procedure employed for esters **122a** was followed using 2-cyclohexen-1-ol (2.203 g, 2.30 mmol), orthoester **119a** (0.630 g, 3.45 mmol) and trimethylacetic acid (0.02 g, 0.2 mmol) in mesitylene (9 mL). After a reflux period of 24 h the solvent was evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm) using 39:1 hexane-ethyl acetate followed by Kugelrohr distillation afforded esters **125a** (0.233 g, 47%) as an apparently homogenous (TLC, silica, 9:1 hexane-ethyl acetate), colorless oil: bp 168°C (water pump); FT-IR ($CHCl_3$, cast) 1732, 1433 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.27-1.43 (m, 1 H), 1.47-1.60 (m, 1 H), 1.68-1.83 (m, 2 H), 1.85-2.07 (m, 3 H), 2.14-2.27 (m, 1 H), 2.46-2.69 (m, 2 H), 2.45 (ddd, J = 6.0, 9.0, 10.5 Hz, 1 H), 3.57-3.67 (m, 1 H), 3.70 (s), 3.75 (s), [both signals (ratio 40:60) together have an area which corresponds to 3 H], 5.47 (dm, J = 9.9 Hz), 5.60 (dm, J = 9.9 Hz), [both signals together have an area which corresponds to 1 H], 5.75-5.94 (m, 1 H); exact mass, *m/z* calcd for $C_{11}H_{17}ClO_2$ 216.0917, found 216.0917.

Methyl (3aα,7aα)-Octahydro-1*H*-indene-1-carboxylate 126 from 125a.



The general procedure for radical cyclization was followed using esters **125a** (0.14 g, 0.42 mmol) in benzene (50 mL), triphenyltin hydride (0.180 g, 0.52 mmol) in benzene (10 mL) and AIBN (10 mg, 0.07 mmol) in benzene (10 mL). After workup, flash chromatography of the residue over silica gel (1 x 15 cm) using 99:1 hexane-ethyl acetate afforded esters **126** (0.036 g, 47%) as an apparently homogenous (TLC, silica, 9:1 hexane-ethyl acetate), colorless oil. The material was characterized by comparison with a sample made by method described on page 123.

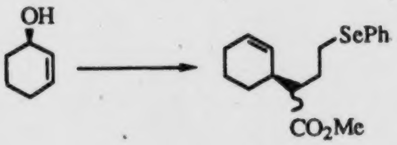
Methyl 2-(2-Cyclohexene-1-yl)-4-bromobutanoate 125b.



The procedure employed for esters **122a** was followed using 2-cyclohexen-1-ol (0.170 g, 1.73 mmol), orthoester **119b** (0.750 g, 3.30 mmol) and trimethylacetic acid (0.025 g, 0.25 mmol) in mesitylene (9 mL). After a reflux period of 24 h the solvent was evaporated. Flash chromatography of the residue over silica gel (2.5

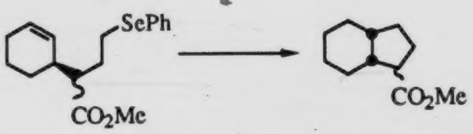
x 15 cm) using 33:1 hexane-ethyl acetate followed by Kugelrohr distillation afforded esters **125b** (0.132 g, 29%) as an apparently homogenous (TLC, silica, 9:1 hexane-ethyl acetate), colorless oil: bp 70°C (0.035 mm); FT-IR ($CHCl_3$, cast) 2934, 1733, 1435, 1260, 1204, 1169 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.18-1.88 (m, 4 H), 1.88-2.14 (m, 2 H), 2.14-2.40 (m, 2 H), 2.40-2.71 (m, 2 H), 3.24-3.57 (m, 2 H), 3.71 (s), 3.75 (s), [both signals together have an area which corresponds to 3 H], 5.40-6.05 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 21.42, 21.58, 24.93, 25.70, 26.76, 27.71, 31.22, 31.51, 31.89, 32.17, 32.62, 37.40, 37.68, 48.51, 48.73, 51.61, 127.68, 128.59, 129.32, 174.51, 174.63; exact mass, *m/z* calcd for $C_{11}H_{17}{}^{79}BrO_2$ 260.0413, found 260.0409.

Methyl 2-(2-Cyclohexen-1-yl)-4-(phenylseleno)butanoate 125c.



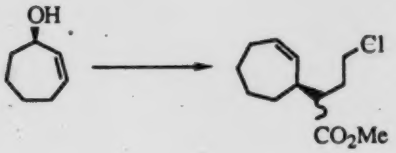
The procedure employed for esters **122a** was followed using 2-cyclohexen-1-ol (0.91 g, 3.03 mmol), orthoester **119c** (1.067 g, 4.70 mmol) and trimethylacetic acid (0.025 g, 0.25 mmol) in mesitylene (6 mL). After a reflux period of 24 h the solvent was evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm) using 33:1 hexane-ethyl acetate gave esters **125c** (0.410 g, 40%) as an apparently homogenous (TLC, silica, 9:1 hexane-ethyl acetate), slightly yellowish oil: FT-IR ($CHCl_3$, cast) 1733 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.207-1.40 (m, 2 H), 1.40-1.60 (m, 1 H), 1.60-2.18 (m, 6 H), 2.34-2.58 (m, 2 H), 2.70-2.82 (m 1 H), 2.86-3.05 (m, 1 H), 3.67 (s), 3.70 (s), [both signals (ratio 70:30) together have an area which corresponds to 3 H], 5.37-5.50 (m, 1 H), 5.67-5.79 (m, 1 H), 7.20-7.30 (m, 3 H), 7.44-7.55 (m, 2 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 21.31, 21.49, 24.93, 25.44, 25.58, 25.72, 25.88, 26.78, 28.99, 29.56, 37.44, 37.67, 47.26, 50.37, 51.39, 51.68, 126.72, 127.96, 128.73, 128.97, 130.06, 131.85, 132.39, 132.45, 132.59, 174.94; exact mass, *m/z* calcd for $C_{17}H_{22}O_2Se$ 338.0785, found 338.0786.

Methyl (3aα,7aα)-Octahydro-1*H*-indene-1-carboxylate 126 from 125c.



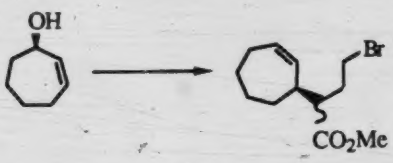
The general procedure for radical cyclization was followed using esters **125c** (0.253 g, 1.17 mmol) in benzene (50 mL), triphenyltin hydride (0.450 g, 1.29 mmol) in benzene (10 mL) and AIBN (10 mg, 0.07 mmol) in benzene (10 mL). After workup, flash chromatography of the residue over silica gel (2.5 x 15 cm) using 75:1 hexane-ethyl acetate followed by Kugelrohr distillation afforded esters **126** (0.155 g, 72%) as an apparently homogenous (TLC, silica, 9:1 hexane -ethyl acetate), colorless oil: bp 80-85°C (1.5 mm); IR (neat) 1729 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.02-2.25 (m, 12 H), 2.62-2.78 (m, 1 H), 2.80-2.96 (m, 2 H), 3.67 (s), 3.70 (s), [both signals together (*ca.* 71:29) have an area which corresponds to 3 H]; exact mass, *m/z* calcd for $C_{11}H_{18}O_2$ 182.1307, found 182.1289.

Methyl 2-(2-Cyclohepten-1-yl)-4-chlorobutanoate 128a.



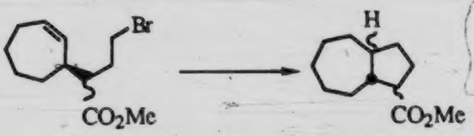
The procedure employed for esters **122a** was followed using 2-cyclohepten-1-ol (0.353 g, 3.15 mmol), orthoester **119a** (0.821 g, 4.50 mmol) and trimethylacetic acid (0.030 g, 0.30 mmol) in mesitylene (9 mL). After a reflux period of 24 h the solvent was evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm) using 33:1 hexane-ethyl acetate gave esters **128a** (0.601 g, 87%) as an apparently homogenous (TLC, silica, 9:1 hexane-ethyl acetate), colorless oil: FT-IR ($CHCl_3$, cast) 1733 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.22-1.38 (m, 2 H), 1.47-1.74 (m, 3 H), 1.84-2.03 (m, 2 H), 2.04-2.29 (m, 3 H), 2.58-2.77 (m, 2 H), 3.43-3.53 (m, 1 H), 3.57-3.67 (m, 1 H), 3.70 {two singlets (ratio 36:64), 3 H}, 5.57-5.66 (m, 1 H), 5.80-5.88 (m, 1 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) (peaks of major isomer only) δ 26.43, 26.56, 28.44, 30.37, 31.44, 31.50, 41.73, 43.49, 47.43, 51.65, 132.77, 133.88; exact mass, *m/z* calcd for $C_{12}H_{19}ClO_2$ 230.1073, found 230.1067.

Methyl 2-(2-Cyclohepten-1-yl)-4-bromobutanoate **128b.**



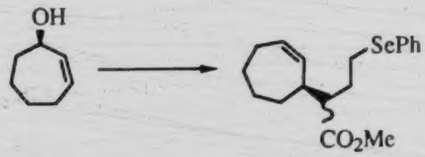
The procedure employed for esters **122a** was followed using 2-cyclohepten-1-ol (0.346 g, 3.10 mmol), orthoester **119b** (0.910 g, 3.10 mmol) and trimethylacetic acid (0.025 g, 0.25 mmol) in mesitylene (9 mL). After a reflux period of 24 h the solvent was evaporated. Flash chromatography of the residue over silica gel (5 x 15 cm) using 33:1 hexane-ethyl acetate followed by Kugelrohr distillation afforded esters **128b** (0.254 g, 30%) as an apparently homogenous (TLC, silica, 9:1 hexane-ethyl acetate), colorless oil: bp 100°C (0.04 mm); FT-IR ($CHCl_3$, cast) 1733, cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.22-1.38 (m, 2 H), 1.47-1.74 (m, 3 H), 1.90-2.23 (m, 4 H), 2.25-2.37 (m, 1 H), 2.59-2.76 (m, 2 H), 3.28-3.38 (m, 1 H), 3.45-3.55 (m, 1 H), 3.68 (s, 3 H), 5.58-5.68 (m, 1 H), 5.78-5.89 (m, 1 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) (peaks of major isomer only) δ 26.52, 28.40, 30.29, 31.45, 31.56, 32.02, 41.65, 48.62, 51.58, 132.71, 133.77, 174.54; exact mass, *m/z* calcd for $C_{12}H_{19}{}^{79}BrO_2$ 274.0569, found 274.0571.

Methyl Decahydro-1-azulenecarboxylate 129 from 128b.



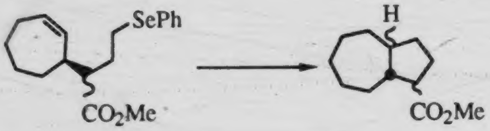
The general procedure for radical cyclization was followed using esters **128b** (0.374 g, 1.06 mmol) in benzene (50 mL), triphenyltin hydride (0.438 g, 1.25 mmol) in benzene (10 mL) and AIBN (10 mg, 0.07 mmol) in benzene (10 mL). After workup, flash chromatography of the residue over silica gel (2.5 x 15 cm) using 99:1 hexane-ethyl acetate followed by Kugelrohr distillation afforded esters **129** (0.163 g, 78%) as an apparently homogenous (TLC, silica, 7:1 hexane-ethyl acetate), colorless oil: bp 72°C (0.25 mm); ^{1}H NMR (CDCl3, 80 MHz) δ 1.05-2.65 (m, 16 H), 2.72-3.13 (m, 1 H), 3.67-3.80 (mainly two s, 3 H); ^{13}C NMR (CDCl3, 100.6 MHz) (indicates two main isomers) δ 27.20, 27.74, 28.65, 29.12, 29.39, 29.71, 30.79, 31.41, 31.53, 31.75, 32.70, 33.08, 33.11, 34.77, 43.56, 43.69, 46.84, 47.51, 50.15, 50.97, 51.38, 52.58, 175.54.

Methyl 2-(2-Cycloheptene-1-yl)-4-(phenylseleno) butanoate 128c.



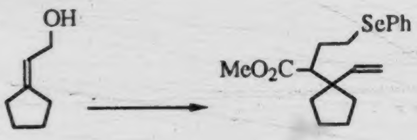
The procedure employed for esters **122a** was followed using 2-cyclohepten-1-ol (0.281 g, 2.55 mmol), orthoester **119c** (1.201 g, 3.95 mmol) and trimethylacetic acid (0.031 g, 0.31 mmol) in mesitylene (9 mL). After a reflux period of 24 h the solvent was evaporated. Flash chromatography of the residue over silica gel (5 x 15 cm) using 33:1 hexane-ethyl acetate followed by Kugelrohr distillation afforded esters **128c** (0.709 g, 79%) as an apparently homogenous (TLC, silica, 9:1 hexane-ethyl acetate), slightly yellowish oil: bp 100°C (0.025 mm); FT-IR ($CHCl_3$, cast) 2922, 1732 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.19-1.35 (m, 2 H), 1.44-1.73 (m, 3 H), 1.77-2.00 (m, 2 H), 2.00-2.21 (m, 3 H), 2.53-2.68 (m, 2 H), 2.73-2.86 (m, 1 H), 2.93-3.04 (m, 1 H), 3.70 (s, 3 H), 5.53-5.65 (m, 1 H), 5.75-5.86 (m, 1 H), 7.20-7.34 (m, 3 H), 7.44-7.56 (m, 2 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 25.63, 25.78, 26.38, 26.49, 28.32, 29.30, 29.71, 30.21, 30.28, 31.31, 41.67, 50.21, 50.59, 51.38, 126.68, 128.95, 130.07, 132.31, 133.80, 133.98, 174.88, 175.04; exact mass, *m/z* calcd for $C_{18}H_{24}O_2Se$ 352.0942, found 352.0945.

Methyl Decahydro-1-azulenecarboxylate 129 from 128c.



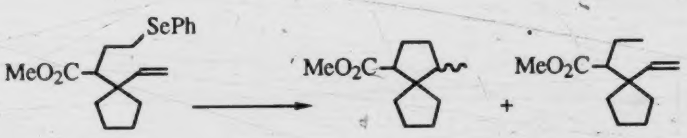
The general procedure for radical cyclization was followed using esters **128c** (0.145 g, 0.63 mmol) in benzene (50 mL), triphenyltin hydride (1.10 g, 3.10 mmol) in benzene (10 mL) and AIBN (25 mg, 0.18 mmol) in benzene (10 mL). After workup, flash chromatography of the residue over silica gel (2.5 x 15 cm) using 99:1 hexane-ethyl acetate afforded esters **129** (0.053 g, 43%) as an apparently homogenous (TLC, silica, 7:1 hexane-ethyl acetate), colorless oil: FT-IR ($CHCl_3$, cast) 1733 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.07-2.05 (m, 14 H), 2.11-2.50 (m 2 H), 2.92 (q, J = 7.5 Hz, 1 H), 3.82-3.86 (4 s, 2 very large, 3 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) (Two main isomers only (^{13}C NMR), major in **bold**) δ **27.15**, **27.70**, **28.62**, 29.08, 29.34, **29.65**, 30.74, **31.35**, 31.47, 31.67, 32.63, **33.01**, **33.06**, 34.70, 43.50, **43.62**, **46.76**, 47.43, **50.05**, **50.88**, 51.29, 52.49, **175.43**; exact mass, *m/z* calcd for $C_{12}H_{20}O_2$ 196.1463, found 196.1461. Anal Calcld for $C_{12}H_{20}O_2$: C, 73.29; H, 10.22. Found: C, 73.51; H, 10.30.

Methyl 2-[(1-Ethenyl)-1-cyclopentyl]-4-(phenylseleno) butanoate 131.



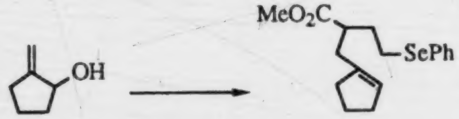
The procedure employed for esters **122a** was followed using $\Delta^{1,\beta}$-cyclopentaneethanol[173] (0.187 g, 1.67 mmol), orthoester **119c** (0.762 g, 2.51 mmol) and trimethylacetic acid (0.017 g, 0.17 mmol) in mesitylene (7 mL). After a eflux period of 24 h the solvent was evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm) using 39:1 hexane-ethyl acetate afforded ester **131** (0.344 g, 58%) as an apparently homogenous (TLC, silica, 9:1 hexane-ethyl acetate), slightly yellowish oil: FT-IR ($CHCl_3$, cast) 1732 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.28-1.37 (m, 1 H), 1.46-1.68 (m, 5 H), 1.68-1.80 (m, 3 H), 2.11 (dddd, J = 4.5, 12.0, 8.5, 3.5 Hz, 1 H), 2.55 (dd, J = 3, 11.25 Hz, 1 H), 2.67 (dt, J = 8, 12.5 Hz, 1 H), 1.92 (ddd, J = 4.8, 8.4, 12.6 Hz, 1 H), 3.66 (s, 3 H), 4.92 (dd, J = 1.5, 18 Hz, 1 H), 5.06 (dd, J = 1.5, 11 Hz, 1 H), 5.76 (dd, J = 17.5, 11 Hz, 1 H), 7.24-7.33 (m, 3 H), 7.47-7.55 (m, 2 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 23.11, 26.17, 26.94, 29.37, 34.86, 34.96, 51.16, 54.44, 113.45, 126.74, 128.98, 130.13, 132.42, 142.04, 174.46; exact mass, *m/z* calcd for $C_{18}H_{24}O_2Se$ 352.0942, found 352.0935.

Cyclization of Methyl 2-[(1-Ethenyl)-1-cyclopentyl]-4-(phenylseleno)butanoate 131.



The general procedure for radical cyclization was followed using ester **131** (0.143 g, 0.40 mmol) in benzene (50 mL), triphenyltin hydride (0.170 g, 0.49 mmol) in benzene (10 mL) and AIBN (10 mg, 0.07 mmol) in benzene (10 mL). After workup, flash chromatography of the residue over silica gel (2.5 x 15 cm) using 99:1 hexane-ethyl acetate followed by Kugelrohr distillation afforded esters **132** and **133** [*ca*. 67:33 (^{1}H NMR)] (0.050 g, 63%) as an apparently homogenous (TLC, silica, 9:1 hexane-ethyl acetate), colorless oil: bp 45°C (0.10 mm); ^{1}H NMR ($CDCl_3$, 80 MHz) δ 0.80-2.76 (m, 16 H), 3.70 (s, 3 H), some olefinic ≈ δ 5-6, which corresponds to ≈ 33% of the product.

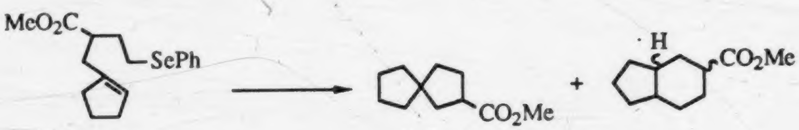
Methyl 2-[(Cyclopenten-1-yl)methyl]-4-(phenylseleno) butanoate 135.



The procedure employed for esters **122a** was followed using 2-methylenecyclopentanol (0.233 g, 2.38 mmol), orthoester **119c** (1.084 g, 3.56 mmol) and trimethylacetic acid (0.024 g, 0.24 mmol) in mesitylene (7 mL). After a reflux period of 24 h the solvent was evaporated. Flash chromatography of the residue over silica gel (5 x 15 cm) using 33:1 hexane-ethyl acetate afforded ester **135** as an apparently homogenous (TLC, silica, 9:1 hexane-ethyl acetate), slightly yellowish oil (0.548 g, 68%); FT-IR ($CHCl_3$, cast) 1736 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.76-1.88 (m, 3 H), 2.01 (dddd, J = 5.5, 9.5, 9.5, 14.7 Hz, 1 H), 2.10-2.29 (m, 5 H), 2.38-2.47 (m, 1 H), 2.74 (ddt, J = 5.0, 10.0, 7.5 Hz, 1 H), 2.82 (ddd, J = 6.5, 9.0, 12.0 Hz, 1 H), 2.94 (ddd, J = 5.2, 9.0, 9.0 Hz, 1 H), 3.68 (s), 3.70 (s), [both signals together have an area which corresponds to 3 H], 5.35-5.39 (m, 1 H), 7.23-7.33 (m, 3 H), 7.46-7.55 (m, 2 H); ^{13}C NMR ($CDCl_3$, 50.3

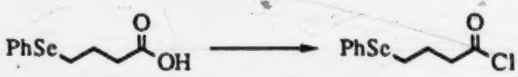
MHz) δ 23.33, 25.05, 32.14, 32.30, 33.54, 34.66, 43.85, 51.38, 125.98, 126.68, 128.88, 129.88, 132.43, 141.04, 175.51; exact mass, *m/z* calcd for $C_{17}H_{22}O_2Se$ 338.0785, found 338.0785.

Cyclization of Methyl 2-[(Cyclopenten-1-yl)methyl]-4-(phenylseleno)butanoate 135.



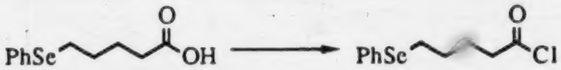
The general procedure for radical cyclization was followed using ester **135** (0.245 g, 0.72 mmol) in benzene (50 mL), triphenyltin hydride (0.317 g, 0.90 mmol) in benzene (10 mL) and AIBN (12 mg, 0.08 mmol) in benzene (10 mL). After workup, flash chromatography of the residue over silica gel (2.5 x 15 cm) using 33:1 hexane-ethyl acetate followed by Kugelrohr distillation afforded esters **136** and **137** [*ca.* 90:10 (^{13}C NMR)] (0.117 g, 87%) as an apparently homogenous (TLC, silica, 9:1 hexane-ethyl acetate), colorless oil: bp 60-62°C (0.25 mm); ^1H NMR ($CDCl_3$, 400 MHz) δ 1.38-1.43 (m, 2 H), 1.46-1.56 (m, 3 H), 1.56-1.66 (m, 5 H), 1.76 (dd, J = 9.1, 12.9 Hz, 2 H), 1.92 (ddd, J = 1.0, 8.5, 12.5 Hz, 2 H), 2.84 (q', J = 8.5 Hz, 1 H), 3.67 (s), 3.69 (s), [both signals (*ca.* 10:90) together have an area which corresponds to 3 H]; ^{13}C NMR ($CDCl_3$, 50.3 MHz) (major product only) δ 24.48, 26.78, 28.76, 29.43, 30.71, 38.50, 38.81, 42.54, 43.00, 51.48, 177.15.

4-(Phenylseleno)butanoyl chloride 142.



Oxalyl chloride (1.440 g, 1 mL, 11.35 mmol) was added dropwise (over about 3 min) to a magnetically stirred solution of 4-(phenylseleno)butanoic acid[176-178] (2.197 g, 9.07 mmol) in dry benzene (10 mL). Stirring at room temperature was continued for 2 h. The solvent was removed under reduced pressure and Kugelrohr distillation of the residue gave **142** (2.324 g, 100%) as a colorless pure (^{1}H NMR) liquid: bp 75-80°C(0.025 mm); FT-IR ($CHCl_3$, cast) 1796 cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 2.11 (q', J = 7 Hz, 2 H), 2.75-3.25 [m, 4 H (including t, J = 7 Hz, at δ 3.08)], 7.27-7.70 (m, 5 H); exact mass, *m/z* calcd for $C_{10}H_{11}OSeCl$ 261.9663, found 261.9661. Anal Calcd for $C_{10}H_{11}OSeCl$: C, 45.91; H, 4.24; O, 6.12. Found: C, 45.76; H, 4.23; O, 6.34.

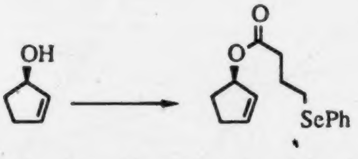
5-(Phenylseleno)pentanoyl chloride 143.



The procedure employed for acid chloride **142** was followed using acid **141**[176-178] (3.240 g, 12.6 mmol) and oxalyl chloride (2.100 g, 15.80 mmol) in dry benzene (25 mL). Kugelrohr distillation gave **143** (3.465 g, 99%) as a pure (^{1}H NMR), colorless oil: bp 90-95°C (0.05 mm); FT-IR ($CHCl_3$, cast) 1788 cm^{-1}; ^{1}H NMR ($CDCl_3$, 199

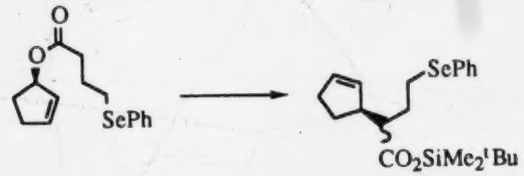
MHz) δ 1.63-1.91 (m, 4 H), 2.78-2.95 (m, 4 H), 7.20-7.32 (m, 3 H), 7.44-7.55 (m, 2 H); exact mass, *m/z* calcd for $C_{11}H_{13}OSeCl$ 275.9821, found 275.9819. Anal Calcd for $C_{11}H_{13}OSeCl$: C, 47.93; H, 4.75; O, 5.81. Found: C, 48.14; H, 4.69; O, 5.97.

2-Cyclopenten-1-yl 4-(Phenylseleno)butanoate 144a.



A solution of 4-(phenylseleno)butanoyl chloride **142** (4.410 g, 16.8 mmol) in dry ether (10 mL) was added dropwise (over about 10 min) to a magnetically stirred solution of 2-cyclopenten-1-ol (0.940 g, 11.2 mmol) and pyridine (3.6 mL, 44.8 mmol) in dry ether (50 mL). Stirring at room temperature was continued overnight, water (50 mL) was added and the aqueous layer was extracted with ether (3 x 50 mL). The combined organic extract was washed with brine (1 x 30 mL), dried (Na_2SO_4) and evaporated. Kugelrohr distillation of the residue gave **144a** (3.403 g, 98%) as a homogenous (TLC, silica, 9:1 hexane-ethyl acetate), colorless oil: bp 110°C (0.025 mm); FT-IR ($CHCl_3$, cast) 1726 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.74-1.86 (m, 1 H), 1.98 (q', J = 7.5 Hz, 2 H), 2.20-2.38 (m, 2 H), 2.40 (t, J = 7.3 Hz, 2 H), 2.44-2.55 (m, 1 H), 2.92 (t, J = 7.3 Hz, 2 H), 5.65-5.72 (m, 1 H), 5.80 (dddd, J = 2.2 Hz, 1 H), 6.08-6.14 (m, 1 H), 7.24-7.35 (m, 3 H), 7.45-7.53 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 25.35, 26.87, 29.69, 30.93, 34.10, 80.35, 126.70, 128.91, 129.21, 129.93, 132.52, 137.30, 172.55; exact mass, *m/z* calcd for $C_{15}H_{18}O_2Se$ 310.0472, found 310.0474. Anal Calcd for $C_{15}H_{18}O_2Se$: C, 58.26; H, 5.87; O, 10.35. Found: C, 58.20; H, 6.02; O, 10.32.

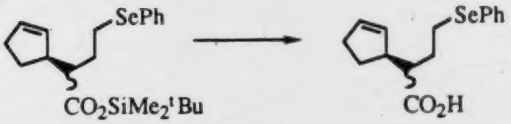
(1,1-Dimethylethyl)dimethylsilyl 2-(2-Cyclopenten-1-yl)-4-(phenylseleno)butanoate 146a.



Lithium diisopropylamide (1.4 mmol) was prepared at 0°C by the addition of *n*-butyllithium (1.55 M in hexane, 0.90 mL, 1.4 mmol) to a solution of diisopropylamine (0.20 mL, 1.40 mmol) in dry THF (3 mL). After about 10 min, the solution was cooled to -78°C and kept at this temperature for 5 min. Ester **144a** (0.388 g, 1.25 mmol) in dry THF (1 mL plus 2 x 0.5 mL rinse) was added very slowly (over about 10 min). The mixture was stirred for 20 min at -78°C. t-Butyldimethylsilyl chloride (0.340 g, 2.26 mmol) and HMPA (0.25 mL, 1.40 mmol) both dissolved together in THF (0.5 mL) were added rapidly dropwise and the reaction mixture was allowed to warm up to 0°C over a period of about 3 h. The solution was then refluxed for 2 h, the solvent was removed under reduced pressure, and Kugelrohr distillation of the residue gave silyl esters **146a** (0.493 g, 93%) as a slightly yellowish oil: bp 112°C (0.015 mm); FT-

IR ($CHCl_3$, cast) 1713 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.256 (s, 3 H), 0.263 (s, 3 H), 0.92 (s, 9 H), 1.42-1.60 (m, 1 H), 1.76-1.90 (m, 1 H), 1.91-2.11 (m, 2 H), 2.21-2.38 (m, 2 H), 2.44 (ddd, J = 7.5, 10.5, 3.5 Hz, 1 H), 2.80 (ddd, J = 7.3, 19.5, 12.5 Hz, 1 H), 2.91-3.04 (m, 2 H), 5.71 (dq, J = 6, 2 Hz, 1 H), 5.76 (dq, J = 6.0, 2.3 Hz), 5.63-5.80 (m), [both signals (ratio 80:20) together have an area which corresponds to 1 H], 7.22-7.31 (m, 3 H), 7.45-7.54 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 17.55, 25.57, 25,73, 27.05, 27.45, 30.50, 30.91, 31.87, 32.08, 47.84, 48.02, 52.20, 52.40, 126.84, 129.02, 130.11, 131.70, 132.02, 132.21, 132.70, 174.85; exact mass, *m/z* calcd for $C_{21}H_{32}O_2SeSi$ 424.1337, found 424.1330.

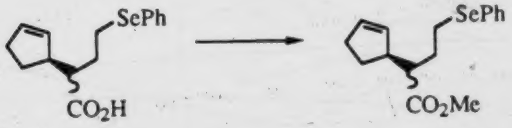
2-(2-Cyclopenten-1-yl)-4-(phenylseleno)butanoic acid 147a.



Tetrabutylammonium flouride (1 M solution in THF, 3 mL, 3 mmol) was added to a magnatecally stirred solution of silyl esters **146a** (0.976 g, 2.30 mmol) in THF (25 mL). The resulting solution was stirred for 15 min at room temperature, acidified with 6*N* HCl (1 mL), diluted with ether (30 mL) and washed with water (2 x 10 mL). The organic layer was dried ($MgSO_4$) and evaporated to afford pure (TLC, silica,, 4:1 hexane-ethyl acetate) acids **147a** (0.698 g, 98%): FT-IR ($CHCl_3$, cast) 3400-2450 (br), 1701 cm^{-1}; ^1H

NMR ($CDCl_3$, 400 MHz) δ 1.48-1.67 (m, 1 H), 1.78-1.92 (m, 1 H), 1.94-2.16 (m, 2 H), 2.22-2.40 (m, 2 H), 2.53 (ddd, J = 3.3, 7.0, 10.3 Hz, 1 H), 2.85 (ddd, J = 7.3, 9.0, 12.5 Hz, 1 H), 2.96-3.12 (m, 2 H), 5.63 (dq, J = 5.5, 2.2 Hz), 5.65 (m), [both signals (ratio 80:20) together have an area which corresponds to 1 H], 5.82 (dq, J = 5.5, 2.2 Hz, 1 H), 7.22-7.38 (m, 3 H), 7.46-7.60 (m, 2 H), 11.33 (very broad s, 1 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 25.38, 25.47, 27.04, 27.58, 29.84, 30.19, 31.87, 32.06, 47.54, 47.80, 50.17, 50.33, 126.88, 129.05, 129.95, 131.18, 131.85, 132.48, 132.60, 132.66, 180.82; exact mass, *m/z* calcd for $C_{15}H_{18}O_2Se$ 310.0472, found 310.0474. Anal Calcd for $C_{15}H_{18}O_2Se$: C, 58.26; H, 5.87; O, 10.35. Found: C, 58.26; H, 5.83; O, 10.47.

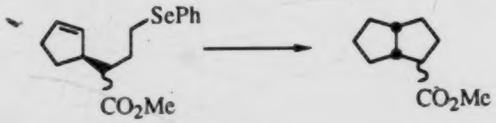
Methyl 2-(2-Cyclopenten-1-yl)-4-(phenylseleno) butanoate 148a.



Diazomethane (unknown molarity in ether) was added dropwise to a magnetically stirred solution of acids **147a** (0.162 g, 0.52 mmol) in ether (10 mL). The addition of diazomethane was continued until the starting acids could no longer be detected (TLC). The solvent was evaporated and Kugelrohr distillation of the residue gave esters **148a** (0.159 g, 94%) as an apparently homogenous (TLC, silica, 7:1 hexane-ethyl acetate), colorless oil: bp 105°C (0.05

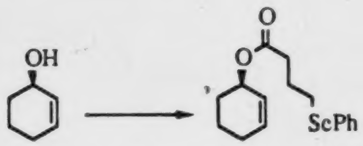
mm); FT-IR ($CHCl_3$, cast) 1733 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.41-1.54 (m, 1 H), 1.76-1.87 (m, 1 H), 1.96 (dtd, J = 16.5, 4.6, 5.2 Hz, 1 H), 2.02-2.13 (m, 1 H), 2.20-2.32 (m, 2 H), 2.43-2.53 (m, 1 H), 2.77 (ddd, J = 7.2, 9.0, 12.5 Hz, 1 H), 2.90-3.00 (m, 2 H), 3.66 (s), 3.68 (s), [both signals (ratio 20:80) together have an area which corresponds to 3 H], 5.59 (dq, J = 5.5, 2.2 Hz), 5.64 (m), [both signals together have an area which corresponds to 1 H], 5.79 (dq, J = 5.0, 2.2 Hz, 1 H), 7.24-7.32 (m, 3 H), 7.46-7.53 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 25.50, 25.57, 27.26, 27.44, 30.35, 30.58, 31.83, 32.03, 47.76, 48.02, 50.46, 51.38, 126.82, 129.02, 130.12, 131.53, 132.05, 132.16, 132.42, 132.56, 132.62, 175.12; exact mass, *m/z* calcd for $C_{16}H_{20}O_2Se$ 324.0628, found 324.0630. Anal Calcd for $C_{16}H_{20}O_2Se$: C, 59.44; H, 6.24; O, 9.90. Found: C, 59.27; H, 6.17; O, 9.69.

Methyl (3aα,6aα)-Octahydro-1-pentalenecarboxylate 149a.



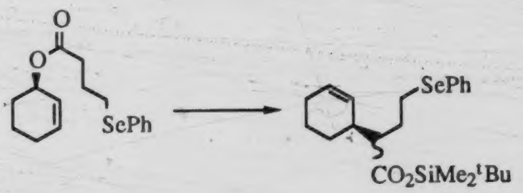
The general procedure for radical cyclization was followed using esters **148a** (0.097 g, 0.30 mmol) in benzene (50 mL), triphenyltin hydride (0.132 g, 0.38 mmol) in benzene (10 mL) and AIBN (5 mg, 0.04 mmol) in benzene (10 mL). After workup, flash chromatography of the residue over silica gel (1 x 15 cm) using 20:1 hexane-ethyl acetate followed by Kugelrohr distillation afforded esters **149a** (0.047 g, 93%) as a colorless oil which was a mixture of the two isomers in a ratio of 80:20 (^{1}H NMR) and was >99% pure (VPC): bp 50°C (2.50 mm); FT-IR (CHCl$_3$, cast) 1730 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz) δ 1.05-1.20 (m, 2 H), 1.24-1.38 (m, 1 H), 1.41-1.51 (m, 1 H), 1.51-1.86 (m, 5 H), 1.86-2.03 (m, 1 H), 2.28-2.38 (m), 2.45-2.60 (m), [both signals together have an area which corresponds to 1 H], 2.60-2.82 (m, 2 H), 3.67 (s), 3.68 (s), [both signals (ratio 20:80) together have an area which corresponds to 3 H]; ^{13}C NMR (CDCl$_3$, 100.6 MHz) (major product) δ 26.50, 27.47, 29.91, 31.89, 34.98, 42.90, 45.67, 48.63, 51.16, 175.02; (minor product) δ 25.42, 31.43, 33.00, 33.45, 33.50, 43.40, 47.88; exact mass (on both isomers), *m/z* calcd for C$_{10}$H$_{16}$O$_2$ 168.1150, found 168.1150.

2-Cyclohexen-1-yl 4-(Phenylseleno)butanoate 144b.



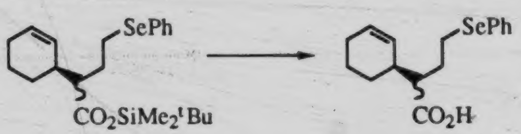
The procedure employed for esters **144a** was followed using 2-cyclohexen-1-ol (1.230 g, 12.50 mmol) and pyridine (3.8 mL, 47.5 mmol) in dry ether (50 mL), and acid chloride **142** (4.103 g, 15.63 mmol). Kugelrohr distillation yielded esters **144b** (3.317 g, 91%) as a homogenous (TLC, silica, 9:1 hexane-ethyl acetate), colorless oil: bp 105°C (0.015 mm); FT-IR (CHCl$_3$, cast) 1729 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz) δ 1.55-1.77 (m, 3 H), 1.78-1.89 (m, 1 H), 1.92-2.12 [m, 4 H (including q', J = 7.25, at δ 2.07)], 2.42 (t, J = 7.25 Hz, 2 H), 2.94 (t, J = 7.25 Hz, 2 H), 5.22-5.29 (m, 1 H), 5.69 (dtt, J = 4.9, 3.5, 1.75 Hz, 1 H), 5.94 (dtd, J = 10, 3.7, 1.0 Hz, 1 H), 7.19-7.28 (m, 3 H), 7.45-7.52 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 18.78, 24.77, 25.43, 26.91, 28.23, 34.24, 68.00, 125.62, 126.76, 128.95, 129.93, 132.52, 132.57, 172.33; exact mass, *m/z* calcd for $C_{16}H_{20}O_2Se$ 324.0628, found 324.0632. Anal Calcd for $C_{16}H_{20}O_2Se$: C, 59.44; H, 6.24; O, 9.90. Found: C, 59.36; H, 6.08; O, 9.54

(1,1-Dimethylethyl)dimethylsilyl 2-(2-Cyclohexen-1-yl)-4-(phenylseleno)butanoate 146b.



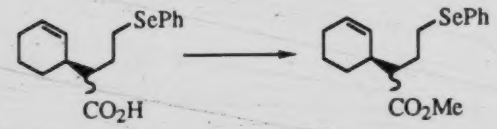
The procedure employed for silyl esters **146a** was followed using lithium diisopropylamide (3.00 mmol) [from *n*-butyllithium (1.55 M, 1.94 mL, 3.00 mmol) and diisopropylamine (0.42 mL, 3.00 mmol)] in THF (3 mL), esters **144b** (0.862 g, 2.66 mmol) in THF (1 mL plus 2 x 0.5 mL rinse), t-butyldimethylsilyl chloride (0.839 g, 5.57 mmol) and HMPA (0.54 mL, 3.00 mmol) in THF (0.5 mL). After a reflux period of 3 h, the solvent was evaporated. Kugelrohr distillation of the residue gave silyl esters **146b** (1.025 g, 88%) as a slightly yellowish oil: bp 115°C (0.02 mm); FT-IR ($CHCl_3$, cast) 1710 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.24 (s, 3 H), 0.25 (s, 3 H), 0.91 (s, 9 H), 1.20-2.15 (m, 9 H), 2.40-2.52 (m, 2 H), 2.76-2.88 (m, 1 H), 2.92-3.05 (m, 1 H), 5.40-5.60 (m, 1 H), 5.68-5.78 (m, 1 H), 7.20-7.30 (m, 3 H), 7.43-7.53 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) (both isomers) δ -4.92, -4.89, 21.32, 21.60, 24.76, 24.93, 25.26, 25.46, 25.72, 25.89, 25.92, 26.62, 28.21, 29.17, 125.57, 126.71, 128.30, 128.71, 128.92, 130.05, 132.53, 132.56, 172.39, 174.64; exact mass, *m/z* calcd for $C_{22}H_{34}O_2SeSi$ 438.1493, found 438.1499. Anal Calcd for $C_{22}H_{34}O_2SeSi$: C, 60.39; H, 7.83. Found: C, 59.02; H, 7.44.

2-(2-Cyclohexen-1-yl)-4-(phenylseleno)butanoic acid 147b.



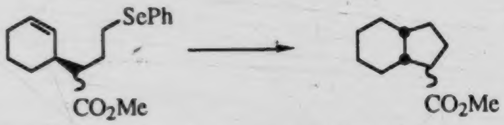
The procedure employed for silyl esters **146a** was followed using silyl esters **146b** (1.079 g, 2.46 mmol) in THF (20 mL), and tertrabutyl-ammonium flouride (1M, 3 mL, 3.00 mmol). Acids **147b** (0.682 g, 85%) were obtained pure (TLC, silica, 4:1 hexane-ethyl acetate), as a yellowish oil: FT-IR ($CHCl_3$, cast) 3600-2400 (br), 1702 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.20-1.34 (m, 1 H), 1.40-1.56 (m, 1 H), 1.65-2.20 (m, 6 H), 2.40-2.59 (m, 2 H), 2.82 (ddd, J = 8.9, 7.4, 12.0 Hz, 1 H), 3.06 (ddd, J = 8.9, 5.0, 12.0 Hz, 1 H), 5.50 (broad d, J = 10 Hz), 5.59 (dd, J = 2, 10 Hz), [both signals (ratio 82:18) together have an area which corresponds to 1 H], 5.72-5.81 (m, 1 H), 7.20-7.36 (m, 3 H), 7.47-7.56 (m, 2 H), 9.65 (very broad s, 1 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) (both isomers) δ 21.35, 21.55, 24.92, 25.00, 25.57, 25.67, 25.75, 26.87, 28.60, 29.28, 37.31, 37.60, 50.20, 50.33, 126.81, 127.67, 128.63, 129.00, 129.25, 130.00, 132.53, 132.60, 180.49; exact mass, *m/z* calcd for $C_{16}H_{20}O_2Se$ 324.0629, found 324.0629. Anal Calcd for $C_{16}H_{20}O_2Se$: C, 59.44; H, 6.24; O, 9.90. Found: C, 59.56; H, 6.45; O, 9.67.

Methyl 2-(2-Cyclohexen-1-yl)-4-(phenylseleno)butanoate 148b.



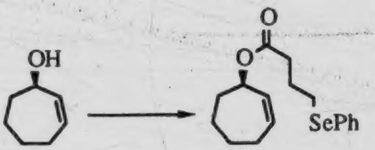
The procedure employed for acids **147a** was followed using acids **147b** (0.487 g, 1.50 mmol) in ether (15 mL) and diazomethane. Kugelrohr distillation afforded esters **148b** (0.482 g, 94%) as an apparently homogenous (TLC, silica, 9:1 hexane-ethyl acetate), colorless oil: bp 103°C (0.015 mm); FT-IR ($CHCl_3$, cast) 1732 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.17-1.32 (m, 1 H), 1.38-1.53 (m, 1 H), 1.59-1.74 (m, 2 H), 1.80 (dddd, J = 3.5, 7.0, 9.5, 14.0 Hz, 1 H), 1.88-1.98 (m, 2 H), 2.08 (dddd, J = 5.2, 9.0, 10.5, 14.0 Hz, 1 H), 2.40-2.54 (m, 2 H), 2.75 (ddd, J = 7.5, 8.5, 12.5 Hz, 1 H), 2.96 (ddd, J = 9, 5, 12 Hz, 1 H), 3.66 (s), 3.67 (s), [both signals (ratio 90:10) together have an area which corresponds to 3 H], 5.41 (dm, J = 10.5 Hz), 5.55 (m), [both signals (ratio 90:10) together have an area which corresponds to 1 H], 5.73 (dq, J = 2.5, 10.5 Hz, 1 H), 7.21-7.31 (m, 3 H), 7.45-7.52 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) (both isomers) δ 21.48, 24.92, 24.98, 25.72, 25.89, 26.78, 29.04, 29.58, 37.65, 50.39, 50.46, 51.32, 126.70, 128.72, 128.88, 128.93, 130.07, 132.42, 132.49, 174.89; exact mass, *m/z* calcd for $C_{17}H_{22}O_2Se$ 338.0786, found 338.0786. Anal Calcd for $C_{17}H_{22}O_2Se$: C, 60.53; H, 6.57; O, 9.49. Found: C, 60.72; H, 6.57; O, 9.32.

Methyl (3aα,7aα)-Octahydro-1-*H*-indene-1-carboxylate 149b.



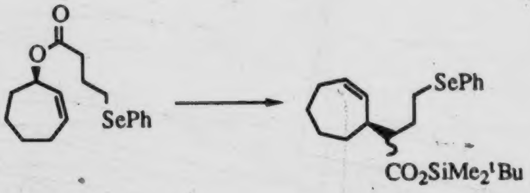
The general procedure for radical cyclization was followed using esters **148b** (0.12 g, 0.36 mmol) in benzene (50 mL), triphenyltin hydride (0.150 g, 0.43 mmol) in benzene (10 mL) and AIBN (5 mg, 0.04 mmol) in benzene (10 mL). After workup, flash chromatography of the residue over silica gel (1 x 15 cm) using 20:1 hexane-ethyl acetate followed by Kugelrohr distillation afforded esters **149b** (0.058 g, 90%) as an apparently homogenous (TLC, silica, 9:1 hexane-ethyl acetate), colorless oil which was a mixture of the two isomers in a ratio of 90:10 (^1H NMR): bp 40°C (0.03 mm); FT-IR ($CHCl_3$, cast) 1737 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.00-1.82 (m, 11 H), 1.98-2.21 (m, 3 H), 2.70 (td, J = 6.2, 9.8 Hz), 3.87 (td, J = 6.2, 9.8 Hz) [both signals together have an area which corresponds to 1 H], 3.655 (s), 3.665 (s), [both signals (ratio 10:90) together have an area which corresponds to 3 H]; ^{13}C NMR ($CDCl_3$, 100.6 MHz) (major product) δ 20.43, 23.11, 23.90, 23.99, 25.12, 25.35, 26.65, 26.97, 27.75, 39.45, 42.56. 48.82, 51.09, 174.74; exact mass, *m/z* calcd for $C_{11}H_{18}O_2$ 182.1306, found 182.1299.

2-Cyclohepten-1-yl 4-(Phenylseleno)butanoate 144c.



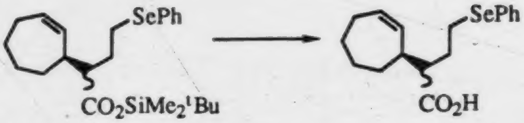
The procedure employed for esters **144a** was followed using 2-cyclohepten-1-ol (1.075 g, 9.60 mmol) and pyridine (2.9 mL, 35.52 mmol) in dry ether (50 mL), and acid chloride **142** (3.150 g, 12.00 mmol). Kugelrohr distillation yielded esters **144c** (2.791 g, 86%) as a homogenous (TLC, silica, 9:1 hexane-ethyl acetate), colorless oil: bp 115°C (0.015 mm); FT-IR ($CHCl_3$, cast) 1730 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.32-1.44 (m, 1 H), 1.57-1.71 (m, 3 H), 1.75-1.85 (m, 1 H), 1.88-1.96 (m, 1 H), 1.97-2.12 [m, 3 H (including t at δ 2.05, J = 7.3 Hz)], 2.13-2.24 (m, 1 H), 2.44 (t, J = 7.3 Hz, 2 H), 2.93 (t, J = 7.5 Hz, 2 H), 5.37-5.46 (m, 1 H), 5.62 (qd, J = 1.5, 11.5 Hz, 1 H), 5.83 (dddd, J = 2.0, 5.3, 9.3, 14.00 Hz, 1 H), 7.21-7.32 (m, 3 H), 7.47-7.54 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 25.46, 26.44, 26.59, 26.99, 28.43, 32.78, 34.28, 74.19, 126.87, 129.04, 129.92, 131.66, 132.70, 133.47, 172.11; exact mass, *m/z* calcd for $C_{17}H_{22}O_2Se$ 338.0783, found 338.0776. Anal Calcd for $C_{17}H_{22}O_2Se$: C, 60.53; H, 6.57; O, 9.49. Found: C, 60.20; H, 6.49; O, 9.50.

(1,1-Dimethylethyl)dimethylsilyl 2-(2-Cyclohepten-1-yl)-4-(phenylseleno)butanoate 146c.



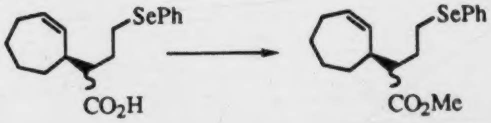
The procedure employed for silyl esters **146a** was followed using lithium diisopropylamide (2.02 mmol) [from *n*-butyllithium (1.55 M, 1.30 mL, 2.02 mmol) and diisopropylamine (0.28 mL, 2.02 mmol)] in THF (3 mL), esters **144c** (0.616 g, 1.82 mmol) in THF (1 mL plus 2 x 0.5 mL rinse), t-butyldimethylsilyl chloride (0.549 g, 3.64 mmol) and HMPA (0.36 mL, 2.07 mmol) in THF (0.5 mL). After an overnight reflux period, the solvent was evaporated. Kugelrohr distillation of the residue gave silyl esters **146c** (0.795 g, 96%) as a slightly yellowish oil: bp 142°C (0.30 mm); FT-IR (CHCl$_3$, cast) 1712 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz) δ 0.22 (s, 3 H), 0.23 (s, 3 H), 0.91 (s, 9 H), 1.20-1.32 (m, 2 H), 1.41-2.20 (m, 8 H), 2.43-2.55 (m, 2 H), 2.79-2.89 (m, 1 H), 3.01-3.09 (m, 1 H), 5.59-5.69 (m, 1 H), 5.78-5.87 (m, 1 H), 7.22-7.32 (m, 3 H), 7.50-7.57 (m, 2 H); ^{13}C NMR (CDCl$_3$, 100.6 MHz) (peaks of major isomer only) δ -4.81, 25.55, 26.11, 26.58, 28.40, 29.43, 30.25, 30.32, 30.38, 41.76, 51.95, 126.74, 128.99, 132.15, 132.51, 132.58, 134.40, 174.74; exact mass, *m/z* calcd for C$_{23}$H$_{36}$O$_2$SeSi 452.1649, found 452.1654. Anal Calcd for C$_{23}$H$_{36}$O$_2$SeSi: C, 61.18; H, 8.04. Found: C, 59.72; H, 7.73.

2-(2-Cyclohepten-1-yl)-4(Phenylseleno)butanoic acid 147c.



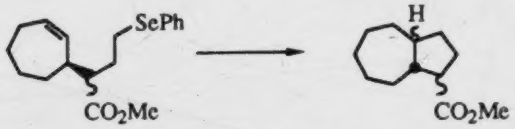
The procedure employed for silyl esters **146a** was followed using silyl esters **146c** (0.721 g, 1.59 mmol) in THF (15 mL), and tertrabutyl-ammonium flouride (1 M, 2 mL, 2.00 mmol). Acids **147c** (0.411 g, 76%) were obtained as an apparently homogenous (TLC, silica, 4:1 hexane-ethyl acetate), yellowish oil: FT-IR ($CHCl_3$, cast) 3600-2400 (br), 1701 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.22-2.22 (m, 10 H), 2.58-2.70 (m, 2 H), 2.80-2.95 (m, 1 H), 3.00-3.15 (m, 1 H), 5.57-5.64 (m, 1 H), 5.77-5.87 (m, 1 H), 7.20-7.33 (m, 3 H), 7.46-7.56 (m, 2 H), 10.7 (very broad s, 1 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) (both isomers) δ 25.73, 25.91, 26.46, 26.58, 28.47, 29.05, 29.36, 29.47, 29.71, 30.24, 30.36, 31.44, 41.66, 50.30, 126.88, 129.09, 132.57, 132.65, 133.55, 133.90, 180.72; exact mass, *m/z* calcd for $C_{17}H_{22}O_2Se$ 338.0785, found 338.0790. Anal Calcd for $C_{17}H_{22}O_2Se$: C, 60.53; H, 6.57; O, 9.49. Found: C, 60.62; H, 6.54; O, 9.72.

Methyl 2-(2-Cyclohepten-1-yl)-4-(phenylseleno)butanoate 148c.



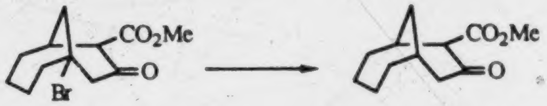
The procedure employed for acids **147a** was followed using acids **147c** (0.372 g, 1.10 mmol) in ether (10 mL) and diazomethane. Kugelrohr distillation afforded esters **148c** (0.382 g, 98%) as an apparently homogenous (TLC, silica, 9:1 hexane-ethyl acetate), colorless oil: bp 110°C (0.05 mm); FT-IR ($CHCl_3$, cast) 1732 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.18-1.33 (m, 2 H), 1.42-1.72 (m, 3 H), 1.81 (dddd, J = 3.7, 7.3, 9.0, 14.0 Hz, 1 H), 1.87-1.99 (m, 1 H), 2.02-2.21 (m, 3 H), 2.54-2.64 (m, 2 H), 2.81 (ddd, J = 12.0, 8.5, 7.3 Hz, 1 H), 3.00 (ddd, 12, 5, 9 Hz, 1 H), 3.69 (s), 3.74 (s), [both signals (ratio 70:30) together have an area which corresponds to 3 H], 5.61 (dm, J = 11 Hz, 1 H), 5.83 (dddd, J = 11, 9, 6, 2 Hz, 1 H), 7.24-7.34 (m, 3 H), 7.47-7.56 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 25.89, 26.53, 28.38, 29.44, 30.15, 30.37, 41.76, 50.35, 51.36, 126.75, 129.00, 131.00, 132.35, 132.46, 133.99, 174.94; exact mass, *m/z* calcd for $C_{18}H_{24}O_2Se$ 352.0941, found 352.0943. Anal Calcd for $C_{18}H_{24}O_2Se$: C, 61.53; H, 6.88; O, 9.11. Found: C, 61.31; H, 6.79; O, 9.31.

Methyl Decahydro-1-azulenecarboxylate 149c.



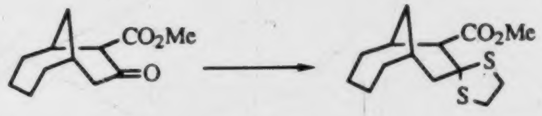
The general procedure for radical cyclization was followed using esters **148c** (0.144 g, 0.41 mmol) in benzene (50 mL), triphenyltin hydride (0.174 g, 0.50 mmol) in benzene (10 mL) and AIBN (10 mg, 07 mmol) in benzene (10 mL). After workup, flash chromatography of the residue over silica gel (1 x 15 cm) using 20:1 hexane-ethyl acetate followed by Kugelrohr distillation afforded esters **149c** (0.057 g, 71%) as an apparently homogenous (TLC, silica, 7:1 hexane-ethyl acetate), colorless oil which was a mixture of four isomers in a ratio of 14:73:11:2 (^{1}H NMR) and was >99% pure (VPC): bp 95°C (1.9 mm); FT-IR ($CHCl_3$, cast) 1735 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.08-1.98 (m, 14 H), 2.14-2.25 (m, 1 H), 2.25-2.43 (m, 1 H), 2.92 (q, J = 7.55 Hz, 1 H), 3.62 (s), 3.64 (s), 3.65 (s), 3.67 (s), [all four signals together have an area which corresponds to 3 H]; ^{13}C NMR ($CDCl_3$, 100.6 MHz) (major isomer in **bold**) δ 26.36, 27.04, **27.20**, 27.37, 27.55, **27.74**, 28.19, **28.65**, 29.11, 29.38, **29.70**, 30.77, **31.40**, 31.52, 31.75, 32.70, **33.06**, **33.11**, 33.27, 33.66, 33.71, 34.25, 34.75, 43.56, **43.69**, 44.75, **46.83**, 47.49, 49.08, 49.20, **50.13**, 50.89, **50.95**, 51.35, 52.56, **175.49**, 176.36; exact mass, *m/z* calcd for $C_{12}H_{20}O_2$ 196.1463, found 196.1465. Anal Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27;. Found: C, 73.50; H, 10.12.

Methyl 8-Oxobicyclo[4.3.1]decane-7-carboxylate 151.



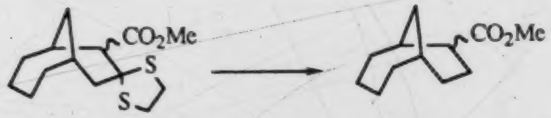
AIBN (5 mg, 0.03 mmol) and triphenyltin hydride (0.660 g, 1.90 mmol) dissolved together in toluene (1 mL) were added to a magnetically stirred solution of methyl 1-bromo-8-oxobicyclo-[4.3.1]decane-7-carboxylate[183b] (0.544g, 1.88 mmol) in toluene (5 mL). The reaction mixture was then refluxed for 24 h. The solvent was evaporated, and the residue was shaken vigorously with ether (25 mL) and a solution of potassium fluoride in water (excess amount was used). The organic layer was dried ($MgSO_4$) and evaporated to give pure (TLC, silica, 9:1 hexane-ethyl acetate) keto esters **151** (0.328 g, 83%) as colorless oil: FT-IR ($CHCl_3$, cast) 1647, 1611 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.20-1.68 (m, 6 H), 1.78 (broad t, J = 3.9 Hz, 2 H), 1.87-2.05 (m, 3 H), 2.23-2.34 (m, 1 H), 2.51 (ddd, J = 18, 7, 1.5 Hz, 1 H), 2.81-2.89 (m, 1 H), 3.75 (s, 3 H), 12.50 (s, 1 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 24.57, 27.18, 28.45, 30.84, 31.75, 33.44, 35.83, 37.32, 51.30, 101.03, 173.21; exact mass, *m/z* calcd for $C_{12}H_{18}O_3$ 210.1256, found 210.1254.

Methyl 8-Oxobicyclo[4.3.1]decane-1-carboxylate ethylene dithioacetal 152.



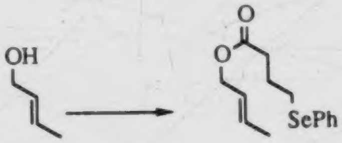
Boron triflouride etherate (0.1 mL, 0.61 mmol) was added to a solution of keto esters **151** (0.328 g, 1.56 mmol) and ethanedithiol (0.440 g, 4.7 mmol) in dichloromethane (7 mL). The mixture was stirred overnight, and the solvent was then evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm) using 9:1 hexane-ethyl acetate afforded pure (^{1}H NMR) **152** (0.406 g, 93%): FT-IR (CHCl3, cast) 1734 cm^{-1}; ^{1}H NMR (CDCl3, 300 MHz) δ 1.35-1.48 (m, 2 H), 1.50-1.70 (m, 5 H), 1.70-1.85 (m, 2 H), 1.97-2.09 (m, 2 H), 2.26-2.37 (m, 1 H), 2.42 (dd, J = 13.5, 9 Hz, 1 H), 2.51-2.61 (m, 1 H), 2.95 (d, J = 6 Hz, 1 H), 3.11-3.37 (m, 4 H), 3.70 (s, 3 H); ^{13}C NMR (CDCl3, 75.5 MHz) δ 26.06, 26.21, 27.33, 29.94, 34.46, 34.57, 35.99, 38.53, 41.00, 48.85, 51.52, 57.17, 66.78, 174.00; exact mass, *m/z* calcd for $C_{14}H_{22}O_2S_2$ 286.1061, found 286.1059.

Methyl Bicyclo[4.3.1]decane-7-carboxylate 150.



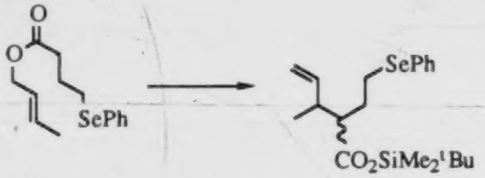
Esters **152** (0.310 g, 1.08 mmol) in dry ethanol (1 mL) were added to a suspension of W5 Raney nickel in ethanol (10 mL). The mixture was refluxed for 4h and then evaporated. Flash chroma-tography of the residue over silica gel (1 x 15 cm) using 4:1 hexane-ethyl acetate gave **150** (0.176 g, 83%) as an apparently homogenous (TLC, silica, 9:1 hexane-ethyl acetate), colorless oil: FT-IR (CHCl3, cast) 1732 cm^{-1}; ^{1}H NMR (CDCl3, 300 MHz) δ 1.21-1.90 (m, 14 H), 1.98-2.09 (m, 1 H), 2.34-2.48 (m, 2 H), 3.68 (s, 3 H); ^{13}C NMR (CDCl3, 75.5 MHz) δ 14.12, 20.85, 22.68, 27.21, 27.26, 28.22, 28.54, 29.25, 31.62, 32.09, 34.04, 34.70, 35.10, 45.31, 51.47, 176.42; exact mass, *m/z* calcd for $C_{12}H_{20}O_2$ 196.1463, found 196.1464.

(E)-2-Butenyl 4-(Phenylseleno)butanoate 154.



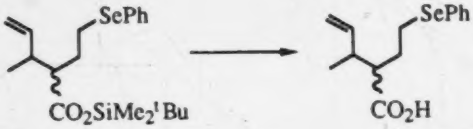
The procedure employed for esters **144a** was followed using crotyl alcohol (0.745 g, 10.35 mmol) and pyridine (2.9 mL, 36.23 mmol) in dry ether (37 mL), and acid chloride **142** (3.397 g, 12.94 mmol). Kugelrohr distillation yielded esters **154** (2.838 g, 92%) as a homogenous (TLC, silica, 7:1 hexane-ethyl acetate), colorless oil: bp 105°C (0.035 mm); FT-IR (CHCl3, cast) 1731 cm^{-1}; ^{1}H NMR (CDCl3, 400 MHz) δ 1.71 (dd, J = 6.5, 1.5, 3 H), 2.01 (q', J = 7.4 Hz, 2 H), 2.49 (t, J = 7.4 Hz, 2 H), 2.95 (t, J = 7.4, 2 H), 4.50 (dt, J = 0.7, 7.5 Hz, 2 H), 5.53-5.64 (m, 1 H), 5.76-5.85 (m, 1 H), 7.23-7.33 (m, 3 H), 7.47-7.55 (m, 2 H); ^{13}C NMR (CDCl3, 100.6 MHz) δ 17.56, 25.41, 26.96, 33.94, 64.98, 125.22, 126.80, 128.97, 130.02, 131.02, 132.68, 172.40; exact mass, *m/z* calcd for $C_{14}H_{18}O_2Se$ 298.0472, found 298.0476. Anal Calcd for $C_{14}H_{18}O_2Se$: C, 56.57; H, 6.10; O, 10.77. Found: C, 56.70; H, 6.09; O, 10.83.

(1,1-Dimethylethyl)dimethylsilyl 3-Methyl-2-[2-(phenyl seleno)ethyl]-4-pentanoate 155.



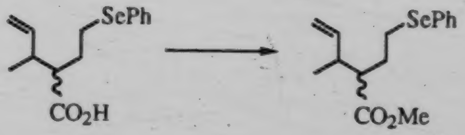
The procedure employed for silyl esters **146a** was followed using lithium diisopropylamide (1.35 mmol) [from *n*-butyllithium (1.55 M, 0.87 mL, 1.35 mmol) and diisopropylamine (0.19 mL, 1.35 mmol)] in THF (3 mL), ester **154** (0.366 g, 1.23 mmol) in THF (1 mL plus 2 x 0.5 rinse), t-butyldimethylsilyl chloride (0.370 g, 2.46 mmol) and HMPA (0.25 mL, 1.35 mmol) in THF (0.5 mL). After an overnight reflux period the solvent was evaporated and Kugelrohr distillation of the residue gave silyl esters **155** (0.473 g, 93%) as a colorless oil: bp 95-100°C (0.025 mm); FT-IR ($CHCl_3$, cast) 1713 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.28 (s), 0.32 (s), (both signals together have an area which corresponds to 6 H), 0.92 (s), 0.94 (s), (both signals together have an area which corresponds to 9 H]), 1.03 (d, J = 6.5 Hz, 3 H), 1.82-2.06 (m, 2 H), 2.35-2.52 (m, 2 H), 2.75-2.84 (m, 1 H), 2.93-3.03 (m, 1 H), 4.97-5.06 (m, 2 H), 5.55-5.85 (m, 1 H), 7.24-7.32 (m, 3 H), 7.46-7.54 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ -4.86, 17.04, 17.50, 18.32, 25.53, 25.66, 25.79, 29.76, 30.71, 39.86, 40.37, 52.61, 52.92, 114.50, 114.97, 126.80, 127.75, 128.94, 130.13, 132.76, 132.84, 141.01, 174.56; exact mass, *m/z* calcd for $C_{20}H_{32}O_2SeSi$ 412.1337, found 412.1365. Anal Calcd for $C_{20}H_{32}O_2SeSi$: C, 58.37; H, 7.84. Found: C, 57.60; H, 7.59.

3-Methyl-2-[2-(Phenylseleno)ethyl]-4-pentanoic acid 156.



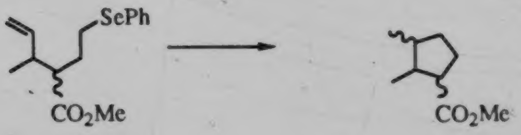
The procedure employed for silyl esters **146a** was followed using silyl esters **155** (0.445 g, 1.08 mmol) in THF (5 mL) and tertra-butylammonium fluoride (1M in THF, 1.5 mL, 1.50 mmol). Acids **156** (0.245 g, 76%) were obtained as an apparently homogenous (TLC, silica, 4:1 hexane-ethyl acetate), yellowish oil: FT-IR ($CHCl_3$, cast) 3600-2400 (br), 1703 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.02 (d, J = 7 Hz), 1.06 (d, J = 6 Hz), [both signals (ratio 16:84) together have an area which corresponds to 3 H], 1.75-2.15 (m, 2 H), 2.40-2.61 (m, 2 H), 2.77-2.88 (ddd, J = 12.5, 9.0, 7.5 Hz, 1 H), 2.96-3.08 (ddd, J = 12.0, 9.5, 5.0 Hz, 1 H), 4.98-5.07 (m, 2 H), 5.62 (ddd, J = 8, 10.2, 17 Hz), 5.77 (ddd, J =m 8, 10.2, 17), [both signals (ratio 20:80) together have an area which corresponds to 2 H], 7.23-7.32 (m, 3 H), 7.47-7.54 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 16.84, 18.33, 25.40, 25.56, 29.11, 30.22, 39.66, 40.19, 50.68, 51.06, 115.06, 115.49, 126.91, 129.03, 129.94, 132.70, 140.54 180.31, 180.63; exact mass, *m/z* calcd for $C_{14}H_{18}O_2Se$ 298.0472, found 298.0478. Anal Calcd for $C_{14}H_{18}O_2Se$: C, 56.57; H, 6.10; O, 10.76. Found: C, 56.81; H, 6.15; O, 10.73.

Methyl 3-Methyl-2-[2-(phenylseleno)ethyl]-4-pentanoate 157.



The procedure employed for acids **147a** was followed using acids **156** (0.164 g, 0.55 mmol) in ether (7 mL) and diazomethane. Kugelrohr distillation afforded pure (^{1}H NMR) esters **157** (0.167 g, 96%) as a colorless oil: bp 75-80°C (0.025 mm); FT-IR ($CHCl_3$, cast) 1734 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.99 (two overlapping d, J = 7 Hz, 3 H), 1.75-2.10 (m, 2 H), 2.34-2.47 (m), 2.48-2.55 (m), [both signals together have an area which corresponds to 2 H], 2.75 (ddd, J = 9.0, 12.0, 7.5 Hz, 1 H), 2.93 (ddd, J = 12.0, 5.0, 9.5 Hz, 1 H), 3.65 (s), 3.68 (s), [both signals (ratio 20:80) together have an area which correspons to 3 H], 4.96-5.07 (m, 2 H), 5.59 (ddd, J = 8,10.2, 17 Hz), 5.72 (ddd, J = 8, 10.2, 17 Hz), [both signals together have an area which corresponds to 1 H], 7.22-7.34 (m, 3 H), 7.46-7.55 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 17.07, 18.34, 25.50, 25.63, 29.52, 30.57, 39.93, 40.45, 51.18, 51.33, 114.63, 115.16, 126.82, 128.98, 130.09, 132.63, 140.93, 174.98; exact mass, *m/z* calcd for $C_{15}H_{20}O_2Se$ 312.0628, found 312.0625. Anal Calcd for $C_{15}H_{20}O_2Se$: C, 57.88; H, 6.48; O, 10.28. Found: C, 57.73; H, 6.37; O, 10.26.

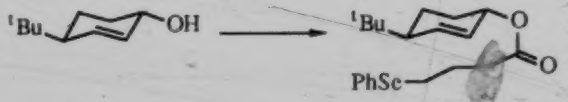
Methyl 2,3-Dimethylcyclopentanecarboxylate 158.



The general procedure for radical cyclization was followed using esters **157** (0.069 g, 0.22 mmol) in benzene (50 mL), triphenyltin hydride (0.096 g, 0.28 mmol) in benzene (10 mL) and AIBN (3 mg, 0.02 mmol) in benzene (10 mL). After workup, Kugelrohr distillation of the residue afforded esters **158** (0.024 g, 69%) as an apparently homogenous (TLC, silica, 9:1 hexane-ethyl acetate), colorless oil which was a mixture of four isomers (^1H NMR): bp 75°C (water pump); FT-IR ($CHCl_3$, cast) 1737 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.695 (d, J = 7 Hz), 0.84 (d, J = 7 Hz), 0.865 (d, J = 7 Hz), 0.91 (d, J = 7 Hz), 0.935 (d, J = 7 Hz), 0.945 (d, J = 7 Hz), 0.995 (d, J = 7 Hz) (first major doublet), 1.03 (d, J = 7 Hz) (second major doublet), (the other six doublets have a low integrals), [all eight signals together have an area which corresponds to 6 H], 1.26-1.50 (m, 2 H), 1.51-2.02 (m, 4 H), 2.06-2.45 (m, 1 H), 3.61 (s), 3.68 (s), [both signals together have an area which corresponds to 3 H]; ^{13}C NMR ($CDCl_3$, 100.6

MHz) (main isomer in **bold**) δ 14.77, 14.90, 15.02, 15.44, **17.28**, **18.07**, 18.68, 23.40, 24.46, 26.96, **27.65**, 29.64, 30.21, 32.77, **33.53**, 40.56, 41.73, **42.55**, **46.66**, 48.10, 49.08, **51.40**, **51.99**, **176.90**; exact mass, *m/z* calcd for $C_9H_{16}O_2$ 156.1150, found 156.1130.

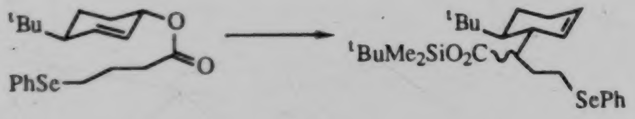
***Trans*-[4-(1,1-Dimethylethyl)-2-cyclohexen-1-yl] 4-(Phenylseleno)butanoate 160.**



The procedure employed for esters **144a** was followed using *trans*-4-(1,1-dimethylethyl)-2-cyclohexen-1-ol[200] **159** (0.920 g, 5.97 mmol) and pyridine (1.5 mL, 17.92 mmol) in dry ether (30 mL), and acid chloride **142** (1.95 g, 7.50 mmol). Kugelrohr distillation yielded ester **160** (2.322 g, 98%) as a homogenous (TLC, silica, 9:1 hexane-ethyl acetate), colorless oil: bp 120-125°C (0.07 mm); FT-IR ($CHCl_3$, cast) 1729 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.87 (s, 9 H), 1.26-1.55 (m, 2 H), 1.77-1.86 (m, 1 H), 1.89-1.96 (m, 1 H), 2.01 (q', J = 7.3 Hz, 2 H), 2.08-2.17 (m, 1 H), 2.43 (t, J = 7.3 Hz, 2 H), 2.94 (t, J = 7.3 Hz, 2 H), 5.26-5.33 (m, 1 H), 5.58-5.64 (m, 1 H), 5.85 (dq, J = 10.5, 2.0 Hz, 1 H), 7.20-7.29 (m, 3 H), 7.47-7.53 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 22.53, 25.52, 27.01, 27.13, 28.89, 33.46, 34.37, 45 77, 70.50, 126.88, 127.96, 129.08, 130.00, 132.68, 133.04, 172.68; exact mass, *m/z* calcd for $C_{20}H_{28}O_2Se$ 380.1254, found

380.1258. Anal Calcd for $C_{20}H_{28}O_2Se$: C, 63.32; H, 7.44; O, 8.43. Found: C, 63.58; H, 7.53; O, 8.25.

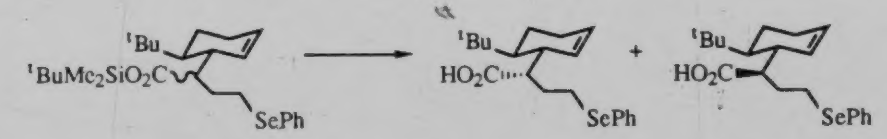
6-(1,1-Dimethylethyl)-α-[2-(phenylseleno)ethyl]-(1SR,6SR)-2-cyclohexene-1-acetic acid (1,1-Dimethylethyl)dimethylsilyl ester 162.



The procedure employed for silyl esters **146a** was followed using lithium diisopropylamide (1.50 mmol) [from *n*-butyllithium (1.60 M, 0.96 mL, 1.50 mmol) and diisopropylamine (0.21 mL, 1.50 mmol)] in THF (3 mL), ester **160** (0.516 g, 1.36 mmol) in THF (1 mL plus 2 x 0.5 mL rinse), t-butyldimethylsilyl chloride (0.410 g, 2.72 mmol) and HMPA (0.30 mL, 1.72 mmol) in THF (0.5 mL). The tetrahydrofuran was evaporated under reduced pressure and replaced by toluene (10 mL). The solution was then refluxed for 14 h and again evaporated under reduced pressure. Kugelrohr distillation of the residue gave silyl esters **162** (0.620 g, 92%) as a slightly yellowish oil: bp 130°C (0.015 mm); FT-IR ($CHCl_3$, cast) 1712 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.24 (s, 3 H), 0.28 (s, 3 H), 0.85 (s, 9 H), 0.93 (s, 9 H), 1.33 (broad t, J = 4.3 Hz, 1 H), 1.40-1.64 (m, 1 H), 1.64-2.20 (m, 6 H), 2.41-2.52 (m, 1 H), 2.73 (ddd, J = 7.8, 8.5, 12.5 Hz, 1 H), 2.96 (ddd, J = 9.3, 12.0, 5.0 Hz, 1 H), 5.47-5.57 (m, 1 H), 5.71-5.82 (m, 1 H), 7.20-7.31 (m, 3 H), 7.43-7.54 (m, 2 H); ^{13}C

NMR ($CDCl_3$, 75.5 MHz) (major isomer) δ -0.86, 17.53, 21.06, 22.67, 25.55, 25.80, 28.91, 31.48, 33.69, 37.51, 42.68, 53.55, 126.97, 128.21, 129.05, 129.32, 129.81, 132.98, 174.93; (minor isomer) δ 21.76, 23.17, 25.89, 26.19, 26.33, 32.12, 37.32, 44.50, 53.08, 126.79, 127.97, 132.65; exact mass (on the mixture of both isomers), *m*/*z* calcd for $C_{26}H_{42}O_2SeSi$ 494.2120, found 494.2120.

6-(1,1-Dimethylethyl)-α-[2-(phenylseleno)ethyl]-(1SR,6SR,αRS)-2-cyclohexene-1-acetic acid 164 and 6-(1,1-Dimethylethyl)-α-[2-(phenylseleno)ethyl]-(1SR,6SR,αSR)-2-cyclohexene-1-acetic acid 165.



The procedure employed for silyl esters **146a** was followed using silyl esters **162** (0.544 g, 1.10 mmol) in THF (7 mL), and tetrabutylammonium flouride (1 M, 2 mL, 2.00 mmol). Acids **163** (0.333 g, 76%) were obtained as a pure (TLC, silica, 4:1 hexane-ethyl acetate), yellowish oil with the two isomers separable. Flash chromatography over silica gel (2.5 x 15 cm) using 8:1 hexane-ethyl acetate gave pure (TLC, silica, 4:1 hexane-ethyl acetate) isomeric materials [0.299 g (90%) of isomer **165** and 0.034 g (10%) of isomer **164**].* (Major product **165**): FT-IR ($CHCl_3$, cast) 1700 cm^{-1}; ^1H

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* These stereochemical assignments are based on NOE and decoupling experiments done on the cyclized products, after the esterification of the acid to the methyl ester (see later). The assignments are also in agreement with

NMR ($CDCl_3$, 400 MHz) δ 0.85 (s, 9 H), 1.32 (broad t, J = 9.5 Hz, 1 H), 1.45-1.57 (m, 1 H), 1.74-1.82 (m, 1 H), 1.82-2.04 (m, 3 H), 2.05-2.17 (m, 1 H), 2.22-2.33 (m, 1 H), 2.58 (ddd, J = 10, 8, 3 Hz, 1 H), 2.74 (dt, J = 12.2, 8.0 Hz, 1 H), 3.05 (ddd, J = 5.0, 16.5, 4.5 Hz, 1 H), 5.53-5.60 (m, 1 H), 5.78-5.86 (m, 1 H), 7.24-7.31 (m, 3 H), 7.46-7.53 (m, 2 H), 12.08 (very broad s, 1 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 21.07, 22.54, 25.73, 28.81, 30.46, 33.70, 37.37, 42.41, 51.52, 126.99, 127.94, 129.09, 129.67, 132.86, 180.67; exact mass, *m/z* calcd for $C_{20}H_{28}O_2Se$ 380.1255, found 380.1255. Anal Calcd for $C_{20}H_{28}O_2Se$: C, 63.32; H, 7.44; O, 8.43. Found: C, 63.60; H, 7.66; O, 8.55.

(Minor product **164**): FT-IR ($CHCl_3$, cast) 1699 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.90 (s, 9 H), 1.21-1.35 (m, 1 H), 1.53-1.73 (m, 2 H), 1.78-2.02 (m, 3 H), 2.02-2.15 (m, 1 H), 2.42-2.49 (broad s, 1 H), 2.68 (ddd, J = 10, 7, 3 Hz, 1 H), 2.81 (ddd, J = 12.0, 8.5, 8.0 Hz, 1 H), 3.05 (ddd, J = 13.5, 8.0, 4.7 Hz, 1 H), 5.53-5.61 (m, 1 H), 5.77-5.85 (m, 1 H), 7.21-7.31 (m, 3 H), 7.46-7.52 (m, 2 H), 12.00 (very broad s, 1 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 2164, 23.10, 25.87, 28.81, 29.03, 29.75, 34.09, 37.09, 44.65, 51.62, 126.92, 127.55, 129.10, 129.78, 129.96, 132.70, 181.12; exact mass, *m/z* calcd for $C_{20}H_{28}O_2Se$ 380.1255, found 380.1260.

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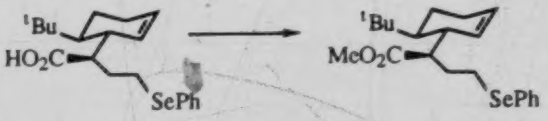
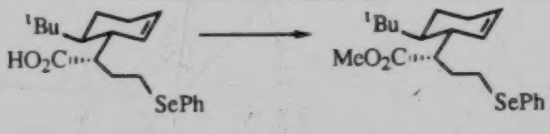
expectation based on the geometry of the silyl ketene acetal **145b** before rearrangment to **146b**.

6-(1,1-Dimethylethyl)-α-[2-(phenylseleno)ethyl]-(1SR,6SR,αRS)-2-cyclohexene-1-acetic acid methyl ester 166.



The procedure employed for acids **147a** was followed using acid **164** (0.022 g, 0.58 mmol) in ether (3 mL) and diazomethane to afford pure (^{1}H NMR) ester **166** (0.021 g, 92%): FT-IR (CHCl$_3$, cast) 1734 cm^{-1}; ^{1}H NMR (CDCl$_3$, 300 MHz) δ 0.88 (s, 9 H), 1.17 (td, J = 2, 5 Hz, 1 H), 1.48-1.62 (m, 1 H), 1.62-1.75 (m, 1 H), 1.75-2.15 (m, 4 H), 2.35-2.41 (m, 1 H), 2.63 (ddd, J = 7.8, 11.0, 3.2 Hz, 1 H), 2.75 (ddd, J = 7.5, 12.5, 9.0 Hz, 1 H), 2.95 (ddd, J = 7.3, 4.8, 9.5 Hz, 1 H), 3.67 (s, 3 H), 5.52-5.61 (m, 1 H), 5.74-5.81 (m, 1 H), 7.19-7.30 (m, 3 H), 7.44-7.50 (m, 2 H); ^{13}C NMR (CDCl$_3$, 75.5 MHz) δ 21.37, 23.02, 25.93, 28.88, 29.75, 33.96, 37.05, 44.45, 51.49, 52.09, 126.86, 127.89, 129.07, 129.37, 132.64, 175.35; exact mass, *m/z* calcd for $C_{21}H_{30}O_2Se$ 394.1411, found 394.1418.

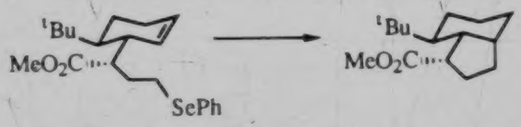
6-(1,1-Dimethylethyl)-α-[2-(phenylseleno)ethyl]-(1SR,6SR,αSR)-2-cyclohexene-1-acetic acid methyl ester 167.



The procedure employed for acids **147a** was followed using acid **165** (0.279 g, 0.74 mmol) in ether (7 mL) and diazomethane.

Kugelrohr distillation afforded pure (^{1}H NMR) ester **167** (0.279 g, 96%) as a homogenous (TLC, silica, 9:1 hexane-ethyl acetate), colorless oil: bp 120°C (0.025 mm); FT-IR (CHCl$_3$, cast) 1733 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz) δ 0.81 (s, 9 H), 1.29 (t, J = 7.8 Hz, 1 H), 1.42-1.53 (m, 1 H), 1.72-2.03 (m, 4 H), 2.05-2.18 (m, 1 H), 2.18-2.25 (m, 1 H), 2.57 (ddd, 10.5, 3.0, 7.5 Hz, 1 H), 2.69 (ddd, J = 8.0, 12.0, 8.5 Hz, 1 H), 2.97 (ddd, J = 13.5, 8.0, 4.5 Hz, 1 H), 3.64 (s, 3 H), 5.43-5.50 (m, 1 H), 5.73-5.81 (m, 1 H), 7.19-7.30 (m, 3 H), 7.42-7.51 (m, 2 H); ^{13}C NMR (CDCl$_3$, 75.5 MHz) δ 21.06, 22.57, 25.97, 28.85, 30.72, 33.80, 37.51, 42.47, 51.39, 51.62, 126.95, 128.28, 129.08, 129.28, 129.94, 132.84, 175.19; exact mass, *m/z* calcd for $C_{21}H_{30}O_2Se$ 394.1411, found 394.1407. Anal Calcd for $C_{21}H_{30}O_2Se$: C, 64.11; H, 7.69; O, 8.13. Found: C, 64.35; H, 7.78; O, 8.12.

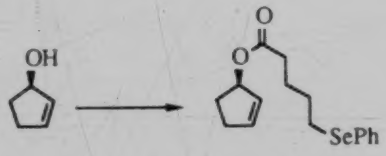
Methyl (1α,3aβ,7β,7aβ)-Octahydro-1-*H*-indene-7-(1,1-dimethylethyl)-1-carboxylate 168.



The general procedure for radical cyclization was followed using ester **167** (0.093 g, 0.237 mmol) in benzene (50 mL), triphenyltin hydride (0.104 g, 0.296 mmol) in benzene (10 mL) and AIBN (5 mg, 0.03 mmol) in benzene (10 mL). After workup, flash chromatography of the residue over silica gel (1 x 15 cm) using 20:1 hexane-ethyl acetate followed by Kugelrohr distillation afforded pure (^{1}H

NMR) **168** (0.043 g, 76%) as a single isomer (^{1}H NMR): bp 95°C (0.025 mm); FT-IR ($CHCl_3$, cast) 1735 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.90 (s, 9 H), 1.26-1.61 (m, 8 H), 1.66-1.86 (m, 2 H), 1.93-2.23 (m, 3 H), 2.93 (ddd, J = 5.2, 9.8, 7.8 Hz, 1 H), 3.66 (s, 3 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 21.53, 22.66, 25.54, 28.60, 28.85, 31.77, 33.90, 37.27, 43.20, 44.29, 48.69, 51.19, 177.25; exact mass, *m/z* calcd for $C_{11}H_{17}O_2$ ($M^{+\cdot}$ - ^{t}Bu) 181.1245, found ($M^{+\cdot}$ - ^{t}Bu) 181.1225. Two NOE experiments were carried out. Irradiation at δ 2.20 produced an enhancement (12.4%) of the signal at δ 2.93; irradiation of the signal at δ 2.93 produced an enhancement (11.4%) of the signal at δ 2.19. Also two decoupling experiments were carried out. Irradiation at δ 2.93 simplified the signals at δ 2.2 and δ 1.8; irradiation at δ 2.2 simplified the signal at δ 2.93.

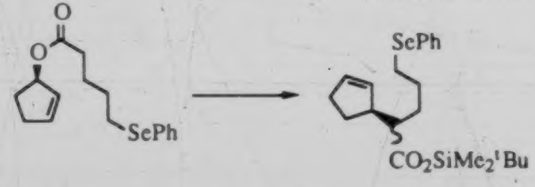
2-Cyclopenten-1-yl 5-(Phenylseleno)pentanoate 170.



The procedure employed for esters **144a** was followed using 2-cyclopenten-1-ol (0.624 g, 7.44 mmol) and pyridine (3.0 mL, 37.20 mmol) in dry ether (40 mL), and acid chloride **143** (2.46 g, 8.93 mmol). Kugelrohr distillation yielded ester **170** (2.31 g, 95%) as a homogenous (TLC, silica, 9:1 hexane-ethyl acetate), colorless oil: bp 110-115°C (0.025 mm); FT-IR ($CHCl_3$, cast) 1729 cm^{-1}; ^{1}H NMR

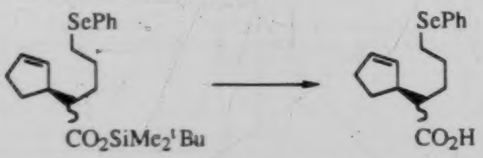
(CDCl3, 400 MHz) δ 1.67-1.84 (m, 5 H), 2.22-2.36 (m, 4 H), 2.45-2.57 (m, 1 H), 2.87-2.97 (m, 2 H), 5.68-5.75 (m, 1 H), 5.80-5.85 (m, 1 H), 6.08-6.13 (m, 1 H), 7.22-7.31 (m, 3 H), 7.47-7.53 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 25.09, 27.27, 29.57, 29.78, 31.04, 33.91, 80.35, 126.70, 128.98, 129.26, 130.27, 132.50, 137.46, 173.19; exact mass, *m/z* calcd for $C_{16}H_{20}O_2Se$ 324.0628, found 324.0624. Anal Calcd for $C_{16}H_{20}O_2Se$: C, 59.44; H, 6.24; O, 9.90. Found: C, 59.34; H, 6.23; O, 10.13.

(1,1-Dimethylethyl)dimethylsilyl 2-(2-Cyclopenten-1-yl)-5-(phenylseleno)pentanoate 171.



The procedure employed for silyl esters **146a** was followed using lithium diisopropylamide (2.20 mmol) [from *n*-butyllithium (1.60 M, 1.37 mL, 2.20 mmol) and diisopropylamine (0.31 mL, 2.20 mmol)] in THF (3 mL), ester **170** (0.648 g, 2.00 mmol) in THF (1 mL plus 2 x 0.5 mL rinse), t-butyldimethylsilyl chloride (0.302 g, 4.00 mmol) and HMPA (0.44 mL, 2.50 mmol) in THF (0.5 mL). After an overnight reflux period, the solvent was evaporated and Kugelrohr distillation of the residue gave silyl esters **171** (0.805 g, 91%) as a slightly yellowish oil: bp 120-125°C (0.05 mm); FT-IR ($CHCl_3$, cast) 1713 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.22 (s), 0.23 (s), 0.24 (s), 0.248 (s), [all four signals together have an area which corresponds to 6 H], 0.91 (s, 9 H), 1.47-1.81 (m, 5 H), 1.95-2.07 (m, 1 H), 2.18-2.41 (m, 3 H), 2.85-2.98 (m, 3 H), 5.57-5.62 (dq, J = 2.0, 5.8 Hz), 5.70-5.75 (m), [both signals (ratio 83:17) together have an area which corresponds to 1 H], 5.77-5.83 (dq, J = 5.5, 2.2 Hz, 1 H), 7.22-7.31 (m, 3 H), 7.46-7.53 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ -4.78, 17.60, 25.63, 27.37, 27.66, 27.76, 28.48, 30.32, 30.64, 31.89, 32.09, 48.18, 48.37, 52.00, 52.11, 126.76, 129.01, 130.51, 131.80, 132.02, 132.11, 132.52, 132.74, 175.24; exact mass, *m/z* calcd for $C_{22}H_{34}O_2SeSi$ 438.1494, found 438.1501.

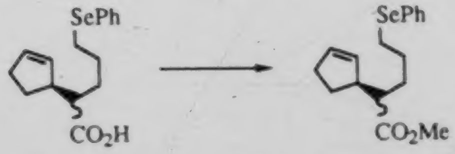
2-(2-Cyclopenten-1-yl)-5-(phenylseleno)pentanoic acid 172.



The procedure employed for silyl esters **146a** was followed using silyl esters **171** (0.799 g, 1.83 mmol) in THF (10 mL) and tetrabutylammonium flouride (1 M, 3 mL, 3.00 mmol). Acids **172** (0.547 g, 92%) were obtained as an apparently homogenous (TLC, silica, 4:1-hexane-ethyl acetate), yellowish oil: FT-IR ($CHCl_3$, cast) 3400-2400 (br), 1702 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.49-1.83 (m, 5 H), 1.98-2.09 (m, 1 H), 2.23-2.41 (m, 3 H), 2.83-3.02 (m, 3 H), 5.63 (dq, J = 6, 2 Hz), 5.72 (dq, J = 6, 2 Hz) [both signals (ratio 81:19) together have an area which corresponds to 1 H], 5.83 (dq, J = 5.5, 2.5 Hz, 1

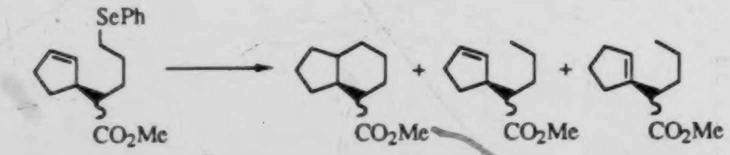
H), 7.22-7.31 (m, 3 H), 7.46-7.53 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) (Major isomer) δ 27.37, 27.72, 28.21, 29.80, 32.12, 48.14, 49.95, 126.86, 129.05, 132.18, 132.31, 132.84, 180.86. (Minor isomer) δ 27.79, 30.08, 31.92, 47.87, 50.06, 130.42, 131.56, 132.64; exact mass, *m/z* calcd for $C_{16}H_{20}O_2Se$ 324.0628, found 324.0633. Anal Calcd for $C_{16}H_{20}O_2Se$: C, 59.44; H, 6.24; O, 9.90. Found: C, 59.57; H, 6.15; O, 9.80.

Methyl 2-(2-Cyclopenten-1-yl)-5-(phenylseleno)pentanoate 173.



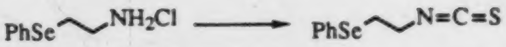
The procedure employed for acids **147a** was followed using acid **172** (0.504 g, 1.56 mmol) in ether (10 mL) and diazomethane. Kugelrohr distillation afforded pure (^1H NMR) esters **173** (0.501 g, 95%) as a colorless oil: bp 110-115°C (0.025 mm); FT-IR ($CHCl_3$, cast) 1733 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.46-1.79 (m, 5 H), 1.92-2.07 (m, 1H), 2.21-2.39 (m, 3 H), 2.84-2.98 (m, 3 H), 3.625 (s), 3.640 (s), [both signals (ratio 17:83) together have an area which corresponds to 3 H], 5.55 (dq, J = 6, 2 Hz), 5.72 (dq, J = 6, 2 Hz), [both signals (ratio 80:20) together have an area which corresponds to 1 H], 5.81 (dq, J = 5.5, 2.2 Hz, 1 H), 7.22-7.33 (m, 3 H), 7.47-7.55 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) (peaks for major isomer only) δ 27.43, 27.52, 28.14, 30.17, 31.97, 48.23, 50.19, 51.25, 126.70, 128.94, 131.94, 132.19, 132.60, 175.60; exact mass, *m/z* calcd for $C_{17}H_{22}O_2Se$ 338.0785, found 338.0789. Anal Calcd for $C_{17}H_{22}O_2Se$: C, 60.53; H, 6.57; O, 9.49. Found: C, 60.59; H, 6.61; O, 9.57.

Reaction of Methyl 2-(2-Cyclopenten-1-yl)-5-(phenylseleno)pentanoate 173 with Triphenyltin hydride.



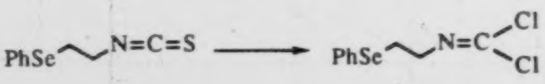
The general procedure for radical cyclization was followed using esters **173** (0.121 g, 0.36 mmol) in benzene (50 mL), triphenyltin hydride (0.160 g, 0.45 mmol) in benzene (10 mL) and AIBN (10 mg, 0.07 mmol) in benzene (10 mL). After workup, Kugelrohr distillation of the residue afforded a mixture consisting of **174** [50% of total (^{1}H NMR)], **175** (11% of total), **176** (39% of total) (0.058 g, 89%) as a colorless oil: bp 70°C (0.035 mm); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.87-0.94 (m), 0.96-1.95 (m), 2.25-2.37 (m), 2.66-2.73 (m), 2.28-2.98 (m), 3.18-3.26 (m), 3.618 (s) (major), 3.633 (s), 3.639 (s), 3.650 (s) (major), 3.659 (s), some very minor olefinic peaks at δ 5.00-6.00.

2-(Phenylseleno)ethylisothiocyanate **179.**[190]



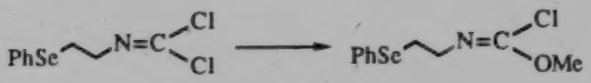
Triethylamine (20 mL, 135.72 mmol) was added dropwise at 0°C to a solution of 2-(phenylseleno)ethylamine hydrochloride (10.70 g, 45.24 mmol) and thiophosgene (6.240 g, 54.3 mmol) in chloroform (100 mL). After completion of the reaction [TLC (3 h)], the mixture was filtered and the solvent was evaporated to give **179** (10.30 g, 94%) as reddish oil: IR ($CHCl_3$) 2173, 2071 (broad and strong) cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 3.07 (t, J = 7 Hz, 2 H), 3.71 (t, J = 7 Hz, 2 H), 7.23-7.50 (m, 3 H), 7.50-7.75 (m, 2 H).

[2-(Phenylseleno)ethyl] carboimidic dichloride **180.**[201]



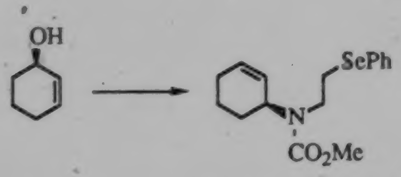
Chlorine was bubbled into a stirred and cooled (below 3°C) solution of isothiocyanate **179** (0.615 g, 2.54 mmol) in dry carbon tetrachloride (15 mL) until no starting material was left [TLC control]. The mixture was then stirred overnight, washed with aqueous sodium sulfite (2 x 10 mL) and saturated aqueous sodium carbonate (2 x 10 mL), dried ($MgSO_4$) and evaporated to give **180** (0.640 g. 89%) as homogenous (TLC, silica, 9:1 hexane-ethyl acetate), yellow oil: FT-IR ($CHCl_3$, cast) 1650 cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 3.07 (t, J = 7 Hz, 2 H), 3.75 (t, J = 7 Hz, 2 H), 7.23-7.45 (m, 3 H), 7.50-7.63 (m, 2 H); exact mass, *m/z* calcd for $C_9H_9NCl_2Se$ 280.9248, found 280.9252.

Methyl 2-(phenylseleno)ethyl carbonochloridimidate 181.[191]



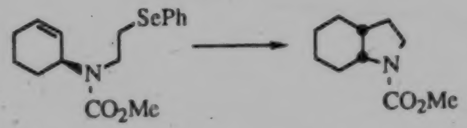
A solution of the carboimidicdichloride **180** (6.479 g, 23.06 mmol) and sodium methoxide (1.370 g, 25.36 mmol) in ether (50 mL) was refluxed for 52 h. The mixture was then filtered and the solvent was evaporated to give virtually pure (^1H NMR) **181** (6.383 g, >99%): FT-IR ($CHCl_3$, cast) 1698 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.06 (t, J = 7 Hz, 2 H), 3.63 (t, J = 7 Hz, 2 H), 3.75 (s, 3 H), 7.20-7.30 (m, 3 H), 7.48-7.57 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 27.79, 51.40, 57.75, 126.88, 129.01, 130.05, 132.61, 140.89; exact mass, *m/z* calcd for $C_9H_{10}ClNSe$ [M - CH_2O] 246.9678, found 246.9693.

Methyl *N*-(2-Cyclohexen-1-yl)-*N*-[2-(phenylseleno)ethyl]-carbamate 183.



2-Cyclohexen-1-ol (0.132 g, 1.35 mmol) in toluene (1 mL plus 2 x 0.5 mL rinse) was added to a suspension of oil-free potassium hydride (0.060 g, 1.50 mmol) in toluene (3 mL). The mixture was stirred for 15 min followed by addition of 18-crown-6 (0397 g, 1.50 mmol) in toluene (7 mL). Stirring at room temp was continued for 30 min and imidoyl chloride **181** (0.472 g, 1.70 mmol) was added. The mixture was refluxed overnight, filtered and evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm) using 9:1 hexane-ethyl acetate gave **183** (0.238 g, 52%) as a homogenous (TLC, silica, 4:1 hexane-ethyl acetate): FT-IR ($CHCl_3$, cast) 1699 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.26-1.46 (broad q, J = 11 Hz, 1 H), 1.46-1.75 (m, 2 H), 1.75-2.03 (m, 3H), 2.88-3.14 (m, 2 H), 3.23-3.47 (m, 2 H), 3.66 (s, 3 H), 4.49-4.78 (m, 1 H), 5.42 (d, J = 9 Hz, 1 H), 5.74-5.85 (m, 1 H), 7.13-7.32 (m, 3 H), 7.45-7.60 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 21.27, 24.42, 26.46, 27.88, 43.99, 52.40, 53.12, 126.91, 127.97, 128.96, 131.62, 132.57, 156.67; exact mass, *m/z* calcd for $C_{16}H_{21}NO_2Se$ 339.0737, found 330.0738. Anal Calcd for $C_{16}H_{21}NO_2Se$: C, 56.81; H, 6.26; N, 4.14; O, 9.46. Found: C, 56.43; H, 6.37; N, 4.07; O, 9.39.

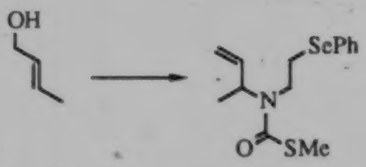
Methyl Octahydroindole-1-carboxylate 184.



The general procedure for radical cyclization was followed using carbamate **183** (0.407 g, 1.20 mmol) in benzene (50 mL), triphenyltin hydride (0.530 g, 1.50 mmol) in benzene (10 mL) and

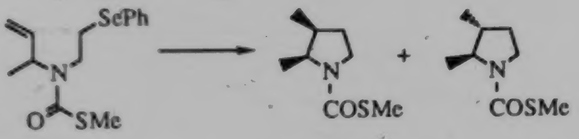
AIBN (12 mg, 0.08 mmol) in benzene (10 mL). Flash chromatography over silica gel 2.5 x 15 cm) using 9:1 hexane-ethyl acetate gave **184** (0.223 g, 100%) as a homogenous (TLC, silica, 4:1 hexane-ethyl acetate), colorless oil: FT-IR ($CHCl_3$, cast) 1702 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.06-1.38 (m, 3 H), 1.38-1.51 (m, 1 H), 1.51-1.76 (m, 4 H), 1.83-2.09 (m, 2 H), 2.14-2.36 (m 1 H), 3.25-3.54 (m, 2 H), 3.60-3.84 [m, 4 H, including a singlet (3 H) at δ 3.67]; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 20.70, 20.98, 23.31, 23.55, 25.90, 26.06, 27.01, 27.20, 27.80, 36.71, 37.39, 44.80, 45.12, 51.78, 56.29, 56.58, 155.08; exact mass, m/z calcd for $C_{10}H_{17}NO_2$ 183.1259, found 183.1259. Anal Calcd for $C_{10}H_{17}NO_2$: C, 65.54; H, 9.35; N, 7.64. Found: C, 65.58; H, 9.46; N, 7.43.

S-Methyl *N*-(Buten-3-yl)-*N*-[2-(phenylseleno)ethyl]thiocarbamate 188.[191]



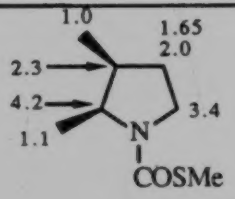
Crotyl alcohol (0.375 g, 5.20 mmol) in THF (1 mL) was added to a suspension of sodium hydride (0.250 g, 60% in oil, 6.25 mmol) in THF (7 mL) at 0°C and the mixture was stirred for 2 h. Isothiocyanate **179** (1.258 g, 5.20 mmol) was added followed by addition of methyl iodide (1.477 g, 10.40 mmol). Stirring was continued for 30 min, the solvent was then evaporated under vacuum and dry xylene (10 mL) was added. The mixture was refluxed for 12 h and then evaporated. Flash chromatography of the residue over silica gel (5 x 15 cm) using 9:1 hexane-ethyl acetate gave **188** (1.185c g, 73 %) as a homogenous (TLC, silica, 4:1 hexane-ethyl acetate), colorless oil: IR ($CHCl_3$) 1640 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.19 (d, J = 6 Hz, 3 H), 2.31 (s, 3 H), 2.91-3.16 (m, 2 H), 3.31-3.51 (m, 2 H), 4.40-5.20 [broad s, (1 H) and m (2 H)], 5.69 (ddd, J = 5, 10, 18 Hz, 1 H), 7.21-7.29 (m, 3 H), 7.47-7.58 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 12.91, 16.85, 44.73, 116.54, 127.04, 129.03, 129.13, 137.29, 168.41; exact mass, *m/z* calcd for $C_{14}H_{19}NOSSe$ 329.0353, found 329.0359.

***Cis-S*-Methyl 2,3-Dimethyl-1-pyrrolidinethiocarboxylate 189 anad *Trans-S*-Methyl 2,3-Dimethyl-1-pyrrolidine thiocarboxylate 190.**

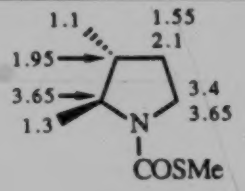


The general procedure for radical cyclization was followed using carbamate **188** (0.40 g, 1.20 mmol) in benzene (50 mL), triphenyltin hydride (0.53 g, 1.50 mmol) in benzene (10 mL) and AIBN (5 mg, 0.03 mmol) in benzene (10 mL). Flash chromatography over silica gel (2.5 x 15 cm) using 19:1 hexane-ethyl acetate gave pure (^1H NMR) **189** (0.130 g, 62.6 %) and pure (^1H NMR) **190**

(0.025 g, 12%). The major isomer **189** had: FT-IR ($CHCl_3$, cast) 1652 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.00 (d, J = 7 Hz, 3 H), 1.06 (d, J = 6 Hz, 3 H), 1.67 (s', J = 10 Hz, 1 H), 1.95 (s', J = 6 Hz, 1 H), 2.27 (octet, J = 6 Hz, 1 H), 2.33 (s, 3 H), 3.23-3.36 (m), 3.39-3.62 (m) [both signals together have an area which corresponds to 2 H], 3.89 (q', J = 7 Hz), 4.17 (q', J = 7 Hz) [both signals together have an area which corresponds to 1 H]; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 12.46, 13.70, 13.90, 14.17, 29.71, 30.64, 35.82, 36.78, 45.27, 46.44, 56.61, 57.45, 166.18; exact mass, *m/z* calcd for $C_8H_{15}NOS$ 173.0875, found 173.0879. The minor isomer **190** had: FT-IR ($CHCl_3$, cast) 1657 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.08 (d, J = 6.8 Hz, 3 H), 1.31 (d, J = 6.3 Hz, 3 H), 1.55 (s', J = 6.5 Hz, 1 H), 1.90-2.02 (m, 1 H), 2.08 (s', J = 6.5 Hz, 1 H), 2.34 (s, 3 H), 3.27-3.45 (m, 1 H), 3.45-3.58 (m, 1 H), 3.58-3.78 (m, 1 H); exact mass, *m/z* calcd for $C_8H_{15}NOS$ 173.0875, found 173.0840. The assignment of stereochemistry of the major and the minor isomers (**189** and **190**, respectively) was based on NOE and decoupling experiments as follows:



189



190

Isomer 189:

I- Decoupling:

1-Irradiation at δ 2.3 made the signal at δ 1.0 collaps to a singlet and also simplified the signals at δ 1.65 and δ 2.0.

2-Irradiation at δ 2.0 simplified the signals at δ 1.65 and δ 2.3.

3-Irradiation at δ 1.1 made the signal at δ 4.2 as a d, J = 7.6 Hz.

4-Irradiation at δ 1.0 simplified the signal at δ 2.3.

II- NOE:

1-Irradiation at δ 1.0 enhanced the signal at δ 2.3 by 10%.

2-Irradiation at δ 1.1 enhanced the signal at 4.2 by 19%.

Isomer 190:

I- Decoupling:

1-Irradiation at δ 1.1 simplified the signal at δ 1.95.

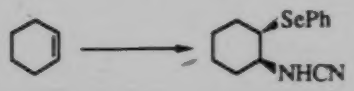
2-Irradiation at δ 1.3 simplified the signals at δ 3.4 and δ 3.65.

II- NOE:

1-Irradiation at δ 1.3 enhanced the signals at δ 3.65 by 11% and at δ 1.95 by 5%.

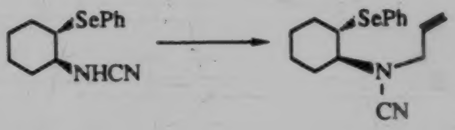
2-Irradiation at δ 1.1 enhanced the signals at δ 3.65 by 11% and at δ 1.95 by 5%.

Trans-[2-(Phenylseleno)cyclohexyl]cyanamide 195.[192]



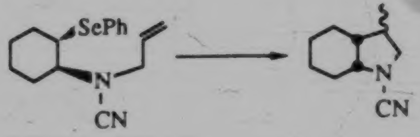
N-(Phenylseleno)phthalimide (1.741 g, 5.77 mmol) in dry dichloromethane (5 ml) was added over 1 h in the dark to a magnetically stirred solution of cyclohexene (0.364 g, 4.43 mmol), freshly distilled [80°C, oil pump vacuum] cyanamide, (3.725 g, 51 mmol) and anhydrous *p*-toluenesulphonic acid[202] (0.763 g, 4.43 mmol) in dry dichloromethane (60 ml). Stirring at room temp was continued for 24 h and the mixture was then filtered and evaporated. Chromatography of the residue over silica gel (5 x 15 cm) using 5:1 hexane-ethyl acetate yielded **195** (0.992 g, 80%) as a homogeneous (TLC, silica, 5:1 hexane-ethyl acetate), slightly yellowish oil: FT-IR ($CHCl_3$, cast) 3207, 3072, 3052, 2939, 2856, 2218, 1477, 1447, 1437, 1022, 742, 691 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.13-1.53 (m, 4 H), 1.55-1.70 (m, 1 H), 1.71-1.82 (m, 1 H), 2.11-2.28 (m, 2 H), 2.78-2.96 (m, 2 H), 4.87 (broad s, 1 H), 7.21-7.38 (m, 3 H) 7.52-7.68 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 24.04, 26.29, 31.63, 33.41, 48.54, 57.08, 114.59, 125.90, 128.42, 129.12, 136.08; exact mass, *m/z* calcd for $C_{13}H_{16}N_2Se$ 280.0479, found 280.0478.

Trans-[2-(Phenylseleno)cyclohexyl](2-propenyl)cyanamide 196.



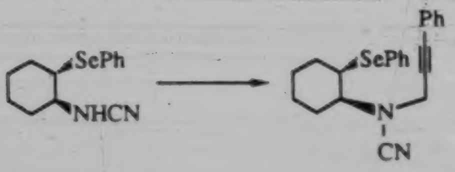
Trans-[2-(Phenylseleno)cyclohexyl]cyanamide **195** (0.356 g, 1.27 mmol) in dry THF (1 ml) and 3-bromo-1-propene (0.192 g, 1.59 mmol) in THF (1 ml) were injected into a stirred suspension of sodium hydride (0.056 g, 60% in oil, 1.71 mmol) in THF (10 ml). Stirring at room temperature was continued overnight and the solvent was then evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm) using 9:1 hexane-ethyl acetate and Kugelrohr distillation (90°C, 0.005 mm) of appropriate fractions gave **196** (0.372 g, 91%) as a homogeneous (TLC, silica, 9:1 hexane-ethyl acetate), slightly yellowish oil: FT-IR ($CHCl_3$, cast) 3062, 3042, 2954, 2843, 2204, 1476, 1443, 1437, 738, 689 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.11-1.35 (m, 2 H), 1.41-1.66 (m, 3 H), 1.77-1.87 (m, 1 H), 2.00-2.20 (m, 2 H), 2.75 (dt, J = 4.25, 11.25 Hz, 1 H), 3.24 (dt, J = 4.25, 11.25 Hz, 1 H), 3.70 (d, J = 6.5 Hz, 2 H), 5.27-5.38 (m, 2 H), 5.86 (dddd, J = 6.5, 6.5, 10.0, 17.0 Hz, 1 H), 7.21-7.37 (m, 3 H), 7.55-7.66 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 24.77, 26.17, 31.80, 34.28, 46.15, 54.37, 63.58, 115.77, 120.35, 127.61, 128.00, 129.00, 131.67, 135.62; exact mass, *m/z* calcd for $C_{16}H_{20}N_2Se$ 320.0792, found 320.0783. Anal. Calcd for $C_{16}H_{20}N_2Se$: C,60.19; H, 6.31; N, 8.77. Found: C, 60.41; H, 6.47; N, 8.62.

(3aα,7aα)-3-Methyloctahydro-1*H*-indole-1-carbonitrile 197.



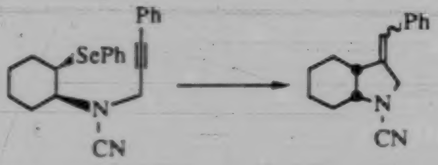
The general procedure for radical cyclization was followed using cyanamide **196** (0.120 g, 0.38 mmol) in benzene (50 ml), triphenyltin hydride (0.164 g, 0.47 mmol) in benzene (10 ml) and AIBN (10 mg, 0.07 mmol) in benzene (10 ml). After evaporation of the reaction mixture, flash chromatography of the residue over silica gel (1 x 15 cm) using 5:1 hexane-ethyl acetate and Kugelrohr distillation (49-51°C, 0.1 mm) yielded **197** [as a mixture of two isomers in a ratio of 61:39 (^{1}H NMR)] (0.06 g, 97%) as an apparently homogeneous (TLC, silica, 5:1 hexane-ethyl acetate), colorless oil: FT-IR ($CHCl_3$, cast) 2924, 2840, 2205 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.88-1.95 [m, 11.5 H, including doublets at δ 0.95 (J = 7 Hz) and at δ 1.02 (J = 7 Hz) in a ratio of 61:39, respectively], 2.04-2.13 (m, 1 H), 2.25-2.42 (m, 0.5 H), 3.01 (dd, J = 5.5, 9 Hz), 3.14 (dd, J = 9, 10.5 Hz), 3.50 (t, J = 9 Hz), 3.64-3.72 (m), [the signals between δ 3.01 and δ 3.72 together correspond to 3 H]; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 11.96, 17.63, 19.97, 21.45, 21.53, 22.38, 23.91, 25.69, 25.85, 27.19, 35.33, 36.52, 40.80, 44.20, 54.37, 56.02, 59.52, 61.20, 116.96, 117.09; exact mass, *m/z* calcd for $C_{10}H_{16}N_2$ 164.1314, found 164.1314. Anal. calcd for $C_{10}H_{16}N_2$: C 73.13; H, 9.82; N, 17.06. Found: C, 73.01; H, 9.71; N, 17.10.

Trans-(3-Phenyl-2-propynyl)[2-(phenylseleno)cyclohexyl] cyanamide 198.



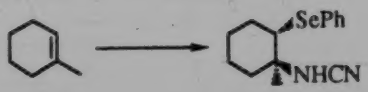
The procedure employed for the allylation of **195** was followed using **195** (0.435 g, 1.55 mmol) in THF (1 ml), 3-bromo-1-propynylbenzene (0.378 g, 1.94 mmol) in THF (1 ml), sodium hydride (0.068 g, 60% in oil, 1.74 mmol) in THF (15 ml) and a reaction time of 3 h. Flash chromatography of the crude product over silica gel (5 x 15 cm) using 5:1 hexane-ethyl acetate gave **198** (0.435 g, 85%) as a homogeneous (TLC, silica, 5:1 hexane-ethyl acetate), slightly yellowish oil: FT-IR ($CHCl_3$, cast) 3045, 2926, 2846, 2209, 1483, 1467, 1434, 1129, 751, 739 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.13-1.37 (m, 2 H), 1.42-1.71 (m, 3 H), 1.78-1.88 (m, 1 H), 2.12-2.29 (m, 2 H), 2.99 (dt, J = 4.2, 11.15 Hz, 1 H), 3.25 (dt, J = 4.2, 11.25 Hz, 1 H), 4.15 (s, 2 H), 7.23-7.38 (m, 6 H), 7.42-7.48 (m, 2 H), 7.62-7.68 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 24.79, 26.19, 31.77, 34.23, 42.33, 46.16, 63.82, 82.07, 86.65, 115.18, 121.99, 127.63, 128.12, 128.39, 128.86, 129.08, 131.81, 135.92; exact mass, *m/z* calcd for $C_{22}H_{22}N_2Se$ 394.0948, found 394.0939. Anal. Calcd for $C_{22}H_{22}N_2Se$: C, 67.19; H, 5.64; N, 7.12. Found: C,66.85; H, 5.79; N, 6.69.

(3aα,7aα)-Octahydro-3-(phenylmethylene)-1*H*-indole-1-carbonitrile 199.



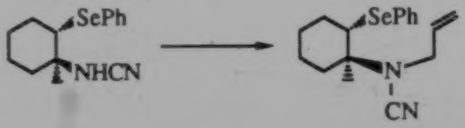
The general procedure for radical cyclization was followed using cyanamide **198** (0.183 g, 0.47 mmol) in benzene (50 ml), triphenyltin hydride (0.204 g, 0.58 mmol) in benzene (10 ml) and AIBN (10 mg, 0.07 mmol) in benzene (10 ml). After evaporation of the reaction mixture, flash chromatography of the residue over silica gel (1 x 15 cm) using 5:1 hexane-ethyl acetate yielded **199** [as a mixture of two isomers in a ratio of 60:40 (^{1}H NMR)] (0.97 g, 87%) as an apparently homogeneous (TLC, silica, 5:1 hexane-ethyl acetate), slightly yellowish oil: FT-IR ($CHCl_3$, cast) 2927, 2849, 2208, 1447 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.21-2.22 (m, 8 H), 2.67-2.77 (m), 2.85-2.96 (m), [both signals together correspond to 1 H and are in a ratio of 40:60, respectively], 3.59-3.70 (m, 1 H), 4.03-4.47 (m, 2 H), 6.28 (broad s), 6.31 (broad s), [both signals together correspond to 1 H and are in a ratio of 60:40, respectively], 7.12-7.40 (m, 5 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 19.62, 20.76, 22.91, 24.12, 25.27, 25.79, 26.23, 27.29, 40.18, 44.61, 51.92, 54.47, 59.67, 60.84, 116.46, 122.59, 122.83, 127.26, 127.97, 128.10, 128.67, 136.50, 139.18, 140.21; exact mass, *m/z* calcd for $C_{16}H_{18}N_2$ 238.1470, found 238.1470. The two isomers were separated by preparative HPLC [Hewlett Packard column of Si-100, 7mm; 100 x 4.6 mm; 1:13 hexane-ethyl acetate; flow rate 2 ml/min]. The major isomer has: ^{1}H NMR ($CDCl_3$, 300 MHz) (characteristic peaks only) δ 2.67-2.76 (m, 1 H), 3.65 (q, J = 7.25 Hz, 1 H), 4.27 (dd, J = 2.2, 14 Hz, 1 H), 4.44 (dm, J = 14 Hz, 1 H), 6.44 (broad s, 1 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 20.74, 22.88, 25.76, 27.27, 44.59, 51.90, 59.65, 116.52, 122.57, 127.20, 128.07, 128.65, 136.39, 139.15; exact mass, *m/z* calcd for $C_{16}H_{18}N_2$ 238.1470, found 238.1465. The minor isomer has: ^{1}H NMR ($CDCl_3$, 300 MHz) (characteristic peaks only) δ 2.18 (dm, J = 14 Hz, 1 H), 2.86-2.95 (m, 1 H), 3.59-3.65 (m, 1 H), 4.08 (dd, J = 1.5, 13.5 Hz, 1 H), 4.40 (dm, J = 13.5, 1 H), 6.31 (broad s, 1 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 19.60, 24.10, 25.25, 26.21, 40.15, 54.45, 60.82, 116.44, 122.81, 127.24, 127.95, 128.61, 136.48, 140.18; exact mass, *m/z* calcd for $C_{16}H_{18}N_2$ 238.1470, found 238.1461.

***Trans*-[1-Methyl-2-(phenylseleno)cyclohexyl]cyanamide 200.**[192]



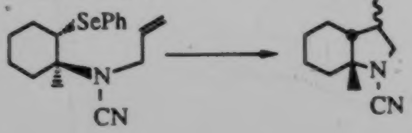
The procedure employed for **195** was followed using 1-methylcyclohexene (0.220 g, 2.20 mmol), cyanamide (1.863 g, 44.36 mmol) and anhydrous *p*-toluenesulphonic acid[202] (0.382 g, 2.20 mmol) in dichloromethane (60 ml), and *N*-(phenylseleno)phthalimide (0.871 g, 2.88 mmol) in dichloromethane (5 ml). Flash chromatography of the crude product over silica gel (2.5 x 15 cm) using 5:1 hexane-ethyl acetate gave **200** (0.534 g, 82%) as a homogeneous (TLC, silica, 5:1 hexane-ethyl acetate), slightly yellowish oil: FT-IR (CHCl3, cast) 3193, 2936, 2210, 1473, 1437, 1390, 1189, 1019, 739, 691 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.16-1.53 (m, 5 H), 1.60-1.84 (m, 4 H), 1.92-2.02 (m, 1 H), 2.08-2.19 (m, 1 H), 3.19 (dd, J = 4, 12 Hz, 1 H) 4.57 (broad s, 1 H), 7.23-7.43 (m, 3 H), 7.55-7.65 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 21.47, 22.22, 26.42, 32.31, 37.29, 55.83, 58.64, 113.78, 127.92, 128.82, 129.26, 134.71; exact mass, *m/z* calcd for $C_{14}H_{18}N_2Se$, 294.0635, found 294.0640.

***Trans*-[1-Methyl-2-(phenylseleno)cyclohexyl](2-propenyl)-cyanamide 200.**



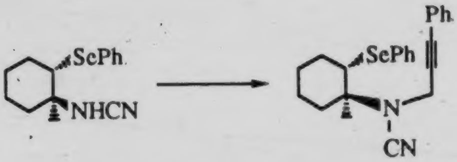
The procedure employed for **196** was followed using **200** (0.50 g, 1.71 mmol) in THF (1 ml), 3-bromo-1-propene (0.261 g, 2.13 mmol) in THF (1 ml), and sodium hydride (0.085 g, 60% in oil, 2.13 mmol) in THF (20 ml). Flash chromatography of the crude product over silica gel (5 x 15 cm) using 5:1 hexane-ethyl acetate and Kugelrohr distillation (99°C, 0.05 mm) gave **201** (0.532 g, 93%) as a homogeneous (TLC, silica, 5:1 hexane-ethyl acetate) oil: FT-IR ($CHCl_3$, cast) 3072, 3052, 2931, 2854, 2201, 1476, 1437, 1383, 1153, 1115, 1023, 927, 740, 693 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.16-1.32 (m, 1 H), 1.36-1.53 (m, 4 H, including singlet at δ 1.41), 1.60-1.87 (m, 5 H), 2.03-2.14 (m, 1 H), 3.44 (dd, J = 4.5, 10.5 Hz, 1 H), 3.50-3.66 (m, 2 H), 5.24-5.36 (m, 2 H), 5.85 (dddd, J = 6.5, 6.5, 10.0, 17.0 Hz, 1 H), 7.22-7.32 (m, 3 H), 7.60-7.78 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 20.02, 22.31, 25.54, 31.60, 36.45, 48.35, 51.87, 62.40, 115.99, 119.58, 127.79, 128.93, 129.07, 132.32, 135.10; exact mass, *m/z* calcd for $C_{17}H_{22}N_2Se$ 334.0948, found 334.0950. Anal. Calcd for $C_{17}H_{22}N_2Se$: C, 61.26; H, 6.65; N, 8.40. Found: C, 61.30; H, 6.55; N, 8.41.

(3aα,7aα)-3,7-Dimethyloctahydro-1*H*-indole-1-carbonitrile 202.



The general procedure for radical cyclization was followed using cyanamide **201** (0.437 g, 1.30 mmol) in benzene (50 ml), triphenyltin hydride (0.574 g, 1.64 mmol) in benzene (10 ml) and AIBN (15 mg, 0.10 mmol) in benzene (10 ml). After evaporation of the reaction mixture, flash chromatography of the residue over silica gel (2.5 x 15 cm) using 5:1 hexane-ethyl acetate and Kugelrohr distillation (65°C, 0.05 mm) yielded **202** [as a mixture of two isomers in a ratio of 60:40 (^{1}H NMR)] (0.221 g, 95%) as an apparently homogeneous (TLC, silica, 5:1 hexane-ethyl acetate), colorless oil: FT-IR ($CHCl_3$, cast) 2932, 2860, 2202 cm^{-1}; ^{1}H NMR (CD_3COOD, 300 MHz) δ 0.95 (d, J = 6.5 Hz), 1.01 (d, J = 6.5 Hz), [both signals together correspond to 3 H], 1.08-1.83 (m, 11 H, including two singlets at δ 1.26 and δ 1.38), 1.93-2.06 (m, 1 H), 2.27-2.46 (m), 2.65-2.81 (m), [both signals together correspond to 1 H and are in a ratio of 40:60, respectively], 3.05 (t, J = 9.5 Hz), 3.15 (t, J = 9.9 Hz), [both signals together correspond to 1 H and are in a ratio of 40:60, respectively], 3.54 (t, J = 9 Hz), 3.64 (t, J = 8.75 Hz), [both signals together correspond to 1 H and are in a ratio of 60:40, respectively]; ^{13}C NMR (CD_3COOD, 75.5 MHz) δ 12.50, 16.17, 21.03, 22.24, 23.23, 23.38, 23.60, 23.95, 24.93, 27.74, 33.81, 34.60, 34.65, 34.88, 46.64, 51.71, 54.57, 56.22, 65.82, 66.67, 116.66, 116.93; exact mass, *m/z* calcd for $C_{11}H_{18}N_2$ 178.1470, found 178.1472. Anal. Calcd for $C_{11}H_{18}N_2$: C, 74.11; H, 10.18; N, 15.71. Found: C, 74.34; H, 10.19; N, 15.71.

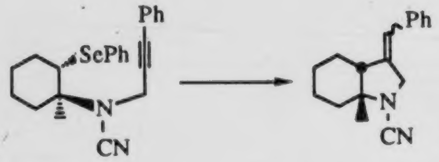
***Trans*-[1-Methyl-2-(phenylseleno)cyclohexyl](3-phenyl-2-propynyl)cyanamide 203.**



The procedure employed for **198** was followed using **200** (0.144 g, 0.49 mmol) in THF (1 ml), 3-bromo-1-propynylbenzene (0.120 g, 0.61 mmol) in THF (1 ml), and sodium hydride (0.022 g, 60% in oil, 0.61 mmol) in THF (15 ml). Flash chromatography of the crude product over silica gel (2.5 x 15 cm) using 5:1 hexane-ethyl acetate gave **203** (0.149 g, 74%) as a homogeneous (TLC, silica, 5:1 hexane-ethyl acetate), slightly yellowish oil: FT-IR ($CHCl_3$, cast) 2937, 2205, 1490, 1437, 1382, 757, 742, 691 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ

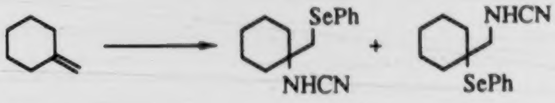
1.19-1.34 (m, 1 H), 1.37-1.56 (m, 4 H, including singlet at δ 1.49), 1.59-2.15 (m, 6 H), 3.48 (dd, J = 4, 10.5 Hz, 1 H), 4.04 (d, J = 4.75 Hz, 2 H), 7.22-7.34 (m, 6 H), 7.37-7.46 (m, 2 H), 7.60-7.68 (m, 2 H); ^{13}C NMR (CDCl$_3$, 75.5 MHz) δ 19.89, 22.40, 25.55, 31.63, 36.54, 37.29, 51.76, 63.19, 83.27, 86.35, 115.62, 122.12, 127.92, 128.30, 128.70, 128.90, 129.17, 131.70, 135.21; exact mass, *m/z* calcd for $C_{23}H_{24}N_2Se$ 408.1105, found 408.1142. Anal. Calcd for $C_{23}H_{24}N_2Se$: C,67.81; H, 5.94; N, 6.88. Found: C, 67.61; H, 5.73; N, 6.68.

(3aa,7aa)-7a-Methyloctahydro-3-(phenylmethylene)-1*H*-indole-1-carbonitrile 204.



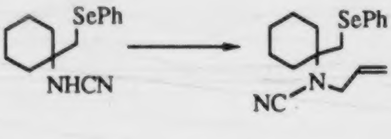
The general procedure for radical cyclization was followed using cyanamide **203** (0.080 g, 0.20 mmol) in benzene (50 ml), triphenyltin hydride (0.086 g, 0.25 mmol) in benzene (10 ml) and AIBN (5 mg, 0.04 mmol) in benzene (10 ml). After evaporation of the solvent, flash chromatography of the residue over silica gel (1 x 15 cm) using 5:1 hexane-ethyl acetate yielded **204** [as a mixture of two isomers in a ratio of 63:37 (^{1}H NMR)] (0.42 g, 85%) as an apparently homogeneous (TLC, silica, 5:1 hexane-ethyl acetate), slightly yellowish oil: FT-IR (CHCl$_3$, cast) 2939, 2859, 2205, 1448, 1324, 736, 695 cm^{-1}; ^{1}H NMR (CDCl$_3$, 300 MHz) δ 1.12-2.17 (m, 11 H, including two singlets at δ 1.15 and δ 1.33), 2.40-2.47 (m), 2.63-2.70 (m), [both signals together correspond to 1 H], 4.06 (dd, J = 1.5, 13.75 Hz, 1 H), 4.28-4.43 (m) [both signals together correspond to 2 H], 6.32-6.36 (bq, J = 2.25 Hz), 6.38 (broad s), [both signals together correspond to 1 H], 7.14-7.40 (m, 5 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 21.27, 22.06, 22.33, 23.49, 24.21, 26.50, 26.69, 27.45, 32.38, 32.69, 46.01, 50.24, 51.03, 53.13, 63.58, 65.22, 122.72, 123.52, 127.17, 127.96, 128.12, 128.36, 128.62, 128.69, 136.48, 136.48, 136.61, 138.72, 140.19; exact mass, *m/z* calcd for $C_{17}H_{20}N_2$ 252.1626, found 252.1626. One isomer was obtained by preparative HPLC [Hewlett Packard column of Si-100, 7mm; 100 x 4.6 mm; 1:13 hexane-ethyl acetate; flow rate 2 ml/min], and had ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.25-1.39 (m, 4 H, including singlet at δ 1.33), 1.43-1.65 (m, 4 H), 1.65-1.83 (m, 3 H), 2.45 (bt, J = 6 Hz, 1 H), 4.35 (m, J = 12.3, 2 H), 6.31-6.36 (m, 1 H), 7.12-7.20 (m, 2 H), 7.20-7.28 (m, 1 H), 7.32-7.40 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 22.04, 22.30, 24.27, 26.86, 32.36, 50.23, 51.01, 63.56, 115.60, 122.71, 127.14, 128.10, 128.67, 136.44, 138.70; exact mass, *m/z* calcd for $C_{17}H_{20}N_2$ 252.1626, found 252.1627.

[1-[(Phenylseleno)methyl]cyclohexyl]cyanamide 205[192] **and [[1-(phenylseleno)cyclohexyl]methyl]cyanamide 205'.**[192]



The procedure employed for **195** was followed using 1-methylcyclohexene (0.263 g, 2.74 mmol), cyanamide (2.300 g, 54.76 mmol) and anhydrous *p*-toluenesulphonic acid[202] (0.420 g, 2.74 mmol) in dichloromethane (50 ml), and *N*-(phenylseleno)phthalimide (1.075 g, 3.56 mmol) in dichloromethane (5 ml). Flash chromatography of the crude product over silica gel (2.5 x 15 cm) using 5:1 hexane-ethyl acetate yielded **205** and **205'** (0.542 g, 67%) as an apparently homogeneous (TLC, silica, 5:1 hexane-ethyl acetate), slightly yellowish oil which was a mixture of **205** and **205'** in a ratio* of *ca*. 92:8 (^{13}C NMR): FT-IR ($CHCl_3$, cast) 3194, 2953, 2859, 2209, 1477, 1447, 730, 691 cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz) (signals for major isomer only) δ 1.25-1.75 (m, 10 H), 3.08 (s, 2 H), 6.90 (broad s, 1 H), 7.15-7.64 (m, 5 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) (signals for major isomer only) δ 21.57, 24.96, 34.71, 41.00, 57.73, 113.76, 127.38, 129.26, 129.95, 133.10; exact mass, *m/z* calcd for $C_{14}H_{19}N_2Se$, 294.0636, found 294.0635.

[1-[(Phenylseleno)methyl]cyclohexyl](2-propenyl)-cyanamide 206.



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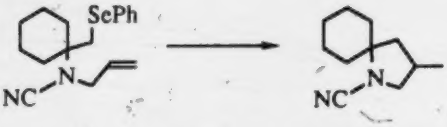
* Our impression is that the ratio is sensitive to the quality of the *N*-(phenylseleno)phthalimide: with pure material a high ratio of 92:8 is obtained.

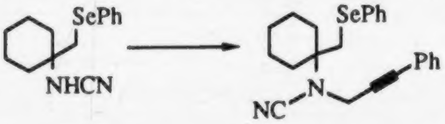
The procedure employed for **196** was followed using a mixture of the isomeric cyanamides **205** and **205'** [*ca*. 92% **205** (^{13}C NMR)] (0.114 g, 0.39 mmol) in THF (1 ml), 3-bromo-1-propene (0.06 g, 0.50 mmol) in THF (1 ml), and sodium hydride (0.020 g, 60% in oil, 0.50 mmol) in THF (10 ml). Flash chromatography of the crude product over silica gel (1 x 15 cm) using 5:1 hexane-ethyl acetate and Kugelrohr distillation (107°C, 0.07 mm) gave **206** (0.102 g, 79%) as a homogeneous (TLC, silica, 5:1 hexane-ethyl acetate), slightly yellowish oil: FT-IR (CHCl$_3$, cast) 2937, 2856, 2202, 1477, 1435, 926, 735, 692 cm^{-1}; ^{1}H NMR (CDCl$_3$, 300 MHz) δ 1.22-1.36 (m, 1 H), 1.45-1.70(m, 7 H), 1.85-1.96 (m, 2 H), 3.12 (s, 2 H), 3.46(dt, J = 1.25, 6.65 Hz, 2 H), 5.23 (dq, J = 1.25, 5.0 Hz, 1 H), 5.29 (q, J = 1.4 Hz, 1 H), 5.83 (ddt, J = 4.13, 9.65, 17.2 Hz, 1 H), 7.22-7.29 (m, 3 H), 7.54-7.62 (m, 2 H); ^{13}C NMR (CDCl$_3$, 75.5 MHz) δ 21.74, 25.07, 33.87, 38.54, 47.98, 61.03, 116.04, 120.28, 127.38, 129.23, 130.32, 131,89, 133.38; exact mass, *m/z* calcd for $C_{17}H_{22}N_2Se$ 334.0942, found 334.0951. Anal. Calcd for $C_{17}H_{22}N_2Se$: C,61.26; H, 6.65; N, 8.40. Found: C, 61.30; H, 6.62; N, 8.35.

3-Methyl-1-azaspiro[4.5]decane-1-carbonitrile 207.



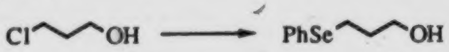
The general procedure for radical cyclization was followed using cyanamide **206** (0.130 g, 0.34 mmol) in benzene (50 ml), triphenyltin hydride (0.177 g, 0.51 mmol) in benzene (10 ml) and AIBN (5 mg, 0.04 mmol) in benzene (10 ml). After evaporation of the solvent, flash chromatography of the residue over silica gel (1 x 15 cm) using 5:1 hexane-ethyl acetate and Kugelrohr distillation (50°C, 0.07 mm) yielded **207** (0.046 g, 66%) as a homogeneous (TLC, silica, 5:1 hexane-ethyl acetate), colorless oil: FT-IR ($CHCl_3$, cast) 2931, 2850, 2202 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.05 (d, J = 6.75 Hz, 3 H), 1.08-1.40 (m, 4 H), 1.49-1.68 (m, 4 H), 1.70-1.84 (m, 3 H), 2.15 (dd, J = 7, 12 Hz, 1 H), 2.20-2.42 (m, 1 H), 3.01 (t, J = 9.5 Hz, 1 H), 3.54 (t, J = 8 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 17.26, 23.92, 24.26, 24.93, 31.91, 35.27, 37.68, 42.65, 56.36, 66.55, 115.97; exact mass, *m/z* calcd for $C_{11}H_{18}N_2$ 178.1470, found 178.1471. Anal. Calcd for $C_{11}H_{18}N_2$: C, 74.11; H, 10.18; N, 15.71. Found: C, 74.05; H, 10.32; N, 15.93.

(3-Phenyl-2-propynyl)[1-[(phenylseleno)methyl] cyclohexyl]-cyanamide 208.



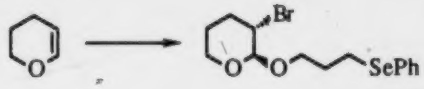
The procedure employed for the cyanamide **198** was followed using a mixture of the isomeric cyanamides **205** and **205'** [in a ratio of 66:34, respectively (^1H NMR)] (0.831 g, 2.83 mmol) in THF (2 ml), 3-bromo-1-propynylbenzene (0.689 g, 3.53 mmol) in THF (1 ml) and sodium hydride (0.124 g, 60% in oil, 3.10 mmol) in THF (20 ml). Flash chromatography of the crude product over silica gel (1 x 15 cm) using 5:1 hexane-ethyl acetate gave **208** and (3-Phenyl-2-propynyl)[[1-(phenylseleno)cyclohexyl]-methyl]cyanamide (0.977 g, 84%). The two isomers were separated by flash chromatography over silica gel (2.5 x 15 cm) using 14:1 hexane-ethyl acetate. The major isomer **208** (0.471 g, 62%, calculated by using the ratio of **205** and **205'** in the starting material) was obtained as a homogeneous (TLC, silica 5:1 hexane-ethyl acetate) white powder and had: FT-IR ($CHCl_3$, cast) 2933, 2857, 2204, 1490, 1477, 1442, 1437, 757, 739, 691 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.20-1.36 (m, 1 H), 1.45-1.77 (m, 7 H), 1.98 (bd, J = 9 Hz, 2 H), 3.29 (s, 2 H), 3.95 (s, 2 H), 7.20-7.37 (m, 6 H), 7.37-7.47 (m, 2 H), 7.53-7.62 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 21.79, 25.04, 33.66, 36.91, 38.48, 61.94, 83.01, 86.60, 115.85, 122.08, 127.40, 128.34, 128.76, 129.25, 130.45, 131.81, 133.34; exact mass, *m/z* calcd for $C_{23}H_{24}N_2Se$ 408.1105, found 408.1126. Anal. Calcd for $C_{23}H_{24}N_2Se$: C, 67.81; H, 5.94; N,6.88; Found: C, 66.92; H, 6.04; N, 6.65. The minor product (0.237 g, 61%, calculated by using the ratio of **205** and **205'** in the starting material) was obtained as a yellowish oil and had: ^1H NMR ($CDCl_3$, 300 MHz) δ 1.17-1.36 (m, 1 H), 1.51-1.76 (m, 7 H), 1.82-1.96 (m, 2 H), 3.36 (s, 2 H), 4.20 (s, 2 H), 7.24-7.40 (m, 6 H), 7.40-7.48 (m, 2 H), 7.62-7.67 (m, 2 H).

3-(Phenylseleno)propanol 215.[195]



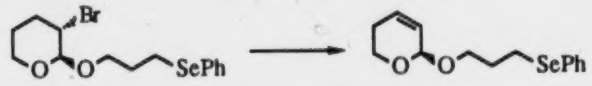
Sodium borohydride (0.127 g, 3.36 mmol) was added in batches to a solution of diphenyl diselenide (0.524 g, 1.68 mmol) in ethanol (10 mL) at 0°C, followed by addition of 3-bromopropanol (0.234 g, 1.68 mmol) in ethanol (2 mL). The mixture was refluxed for 3 h, filtered and evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm) using 5:1 hexane-ethyl acetate gave **215** (0.625 g, 86%) as as a homogenous (TLC, silica, 19:1 hexane-ethyl acetate), yellow oil: FT-IR ($CHCl_3$, cast) 3330 (broad) cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 1.70-2.25 [(m, 3 H, (2 H after D_2O exchange)], 3.00 (t, J = 7 Hz, 2 H), 3.74 (t, J = 6 Hz, 2 H), 7.10-7.65 (m, 5H); exact mass, *m/z* calcd for $C_5H_{12}O_2Se$ 216.0054, found 216.0048.

Trans-3-Bromo-2-[3(phenylseleno)propyloxy]tetrahydropyran 216.



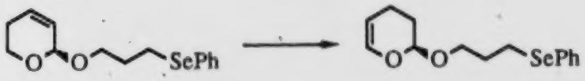
Bromine (0.394 g, 2.45 mmol) was added dropwise at -78°C to a stirred solution of dihydropyran (0,207 g, 2.45 mmol) in ether (10 mL). Then a solution of 3-(phenylseleno)propanol **215** (0.54 g, 2.46 mmol) and pyridine (0.2 mL, 2.46 mmol) in ether (3 mL) was added and the mixture was stirred overnight. The solvent was evaporated and flash chromatography of the residue over silica gel (2.5 x 15 cm) using 9:1 hexane-ethyl acetate gave **216** (0.748 g, 80%) as a homogenous (TLC, silica, 9:1 hexane-ethyl acetate) oil: FT-IR ($CHCl_3$, cast) 3072, 3052, 2931, 2867, 1475, 1437, 1130, 1092, 1071, 1023, 734, 687 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.45-2.43 (m, 7 H), 3.02 (t, J = 7.25 Hz), 3.08 (t, J = 7.25 Hz) [both signals together have an area which corresponds to 2 H], 3.40-3.62 (m, 2 H), 3.71-3.97 (m), 4.02-4.10 (m) [both signals together have an area which corresponds to 3 H], 4.53 (d, J = 5 Hz), 4.67 (d, J = 3 Hz) [both signals together have an area which corresponds to 1 H], 7.13-7.33 (m, 3 H), 7.42-7.55 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 23.73, 24.19, 29.95, 30.58, 49.43, 62.89, 67.43, 101.44, 126.66, 128.94, 130.14, 132.41; exact mass, *m/z* calcd for $C_{14}H_{19}O_2BrSe$ 377.9734, found 377.9726.

2-[3-(Phenylseleno)propyloxy]-2*H*-5,6-dihydropyran 217.



1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) (0.088 g, 0.58 mmol) in dimethyl sulfoxide (1 mL) was added to a solution of **216** (0.219 g, 0.58 mmol) in dimethyl sulfoxide (2 mL) at 90 °C. Heating with stirring was continued for 20 h and then the mixture was evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm) using 12:1 hexane-ethyl acetate gave **217** (0.1411 g, 82%) as a homogenous (TLC, silica, 9:1 hexane-ethyl acetate) oil: FT-IR ($CHCl_3$, cast) 3072, 3052, 2917, 2871, 1480, 1440, 1104, 1071, 1038, 1023, 1008, 738, 687 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.46-2.12 (m, 3 H), 2.21-2.35 (m, 1 H), 3.00 (t, J = 7 Hz, 2 H), 3.47-3.60 (m, 1 H), 3.69 (ddd, J = 11, 6.2, 1.75 Hz, 1 H), 3.81-3.97 (m), 4.03-4.20 (m) [both signals together have an area which corresponds to 2 H], 4.83-4.87 (m, 1 H), 5.70 (dtd, J = 10, 1.5, 2.8 Hz, 1 H), 5.98-6.16 (m, 1 H), 7.16-7.28 (m, 3 H), 7.43-7.55 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 24.58, 24.68, 30.37, 57.26, 66.87, 93.92, 125.75, 126.68, 128.94, 129.00, 130.29, 132.53; exact mass, *m/z* calcd for $C_{14}H_{18}O_2Se$ 298.0472, found 298.0475.

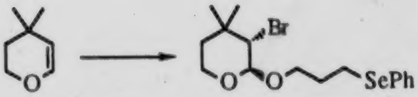
2-[3-(Phenylseleno)propyloxy]-2H-3,4-dihydropyran 218.



Allylic acetal **217** (0.128 g, 0.43 mmol) in ethanol (1 mL) was added to a solution of 1,4-diazabicyclo[2.2.2]octane (DABCO) (0.10 g, 0.87 mmol), tris(triphenylphosphine)rhodium(I) chloride (0.028 g, 0.03 mmol) in 9:1 ethanol-water (3 mL). The mixture was refluxed for 70 h and then evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm) using 9:1 hexane-ethyl acetate to give **218** (0,047 g, 36%) as a homogenous (TLC, silica, 9:1 hexane-ethyl acetate) oil: FT-IR ($CHCl_3$, cast) 3052, 2933, 2867, 1652, 1478, 1437, 1224, 1117, 1059, 1033, 735, 689 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.67-2.03 (m, 5 H), 2.06-2.21 (m, 1 H), 2.99 (td, J = 2.1, 7.5 Hz, 2 H), 3.60 (dt, J = 6, 10 Hz, 1 H), 3.88 (dt, J = 6, 10 Hz, 1 H), 4.72-

4.78 (m, 1 H), 4.93 (t, J = 3.2 Hz, 1 H), 6.20 (td, J = 1.9, 6.25 Hz, 1 H), 7.17-7.30 (m, 3 H), 7.46-7.54 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 16.22, 24.40, 26.77, 30.37, 67.17, 97.04, 101.62, 126.71, 129.03, 130.42, 132.47; exact mass, *m/z* calcd for $C_{14}H_{18}NO_2Se$ 298.0471, found 298.0471.

***Trans*-3-Bromo-4,4-dimethyl-2-[3-(phenylseleno)propyloxy] tetrahydropyran 220.**



4,4-Dimethyldihydropyran **219**[196] (0.075 g, 0.67 mmol) in dichloromethane (1 mL) was added to a magnetically stirred solution of 3-(phenylseleno)propanol (0.329 g, 1.53 mmol) and N-bromosuccinimide (0.1 g, 0.54 mmol) in dichloromethane (7 mL) at -20°C. The mixture was stirred for 2 h while being allowed to warm up to -5°C. Stirring at room temp was continued overnight and the mixture was evaporated. Flash chromatography of the residue over silica gel (1 x 15 cm) using 9:1 hexane-ethyl acetate gave **220** (0.078 g, 37%) as a homogenous (TLC, silica, 9:1 hexane-ethyl acetate) oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.09 (s, 3 H), 1.12 (s, 3 H), 1.54-1.78 (m, 2 H), 1.90-2.13 (m, 2 H), 3.05 (t, J = 7.5 Hz, 2 H), 3.55-3.73 (m, 3 H, including d, J = 8 Hz at δ 3.66), 3.80-3.96 (m, 2 H), 4.50 (d, J = 8 Hz, 1 H), 7.16-7.28 (m, 3 H), 7.45-7.54 (m, 2 H); ^{13}C NMR

(CDCl$_3$, 75.5 MHz) δ 22.44, 24.21, 30.16, 30.56, 35.63, 39.33, 61.28, 64.00, 68.56, 100.63, 126.64, 128.98, 130.19, 132.43.

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